NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM

VOLUME I

NATIONAL HEART AND LUNG INSTITUTE SUMMARY

MAY 1, 1973

NATIONAL HEART AND LUNG INSTITUTE/NATIONAL INSTITUTES OF HEALTH
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

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National Heart, Blood Vessel, Lung and Blood Program

VOL., NOS., YEAR, ETC.

Volumes I, II and III

May 1973

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July 24, 1973

Honorable Spiro T. Agnew
President of the Senate
Washington, D.C. 20510

Dear Mr. President:

The National Heart, Blood Vessel, Lung and Blood Act of 1972 (Public Law 92-423, 86 STAT 679) requires that the Director of the National Heart and Lung Institute submit to Congress a plan for a National Heart, Blood Vessel, Lung and Blood Disease Program. In accordance with this requirement, I am transmitting the report which has been developed by the Director of the National Heart and Lung Institute.

I believe that it is important to note that the report has not been fully reviewed within the Executive Branch. As written, it does not reflect a consideration and development of priorities among all of our research objectives but is limited to those within the scope of the National Heart and Lung Institute. The potential danger of looking at only a single research area is illustrated by the fact that the plan's recommendations for heart and lung research, if implemented within the approved 1974 budget levels, would result in a reduction of $46 million in other important research fields and, consequently, a potential imbalance. Although the plan's resource projections may illustrate the relative priorities between research on arteriosclerosis as opposed to emphysema, the value of those projections is necessarily limited by the failure of the report to consider adequately the appropriate overall level for even the National Heart and Lung Institute in the context of the entire spectrum of biomedical research. It is precisely this problem of an overall balance in our national research efforts that both the Congress and the Executive Branch should have an opportunity to consider in their deliberations and decisions during the annual appropriations process.

In order to respond to the wishes of the Congress for prompt submission, I am transmitting the plan at this time with the above understanding.

Sincerely,

Acting Secretary

Enclosure

July 24, 1973

Honorable Carl Albert
Speaker of the House of
Representatives
Washington, D.C. 20515

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U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

PREFACE

Progress in medical research and treatment of disease is making it increasingly possible to better serve the health needs of our nation. This is especially true in the prevention and control of heart and blood vessel, lung and blood diseases and in the management of blood resources. Nevertheless, diseases of the heart, blood vessels, lung, and blood are collectively the number one cause of death and disability in the nation.

Recognition of the magnitude of the problem, as well as the potential for advancement against these diseases, led to enactment of the *National Heart, Blood Vessel, Lung, and Blood Act of 1972*. As noted in Section 2 (a) (2) of the Act, "elimination of heart and blood vessel diseases [alone] as significant causes of disability and death could increase the average American's life expectancy by about eleven years. . . ."

The Act calls upon the Director of the National Heart and Lung Institute, with the advice of Council, to develop a plan for a National Program which will expand, intensify and coordinate activities in an accelerated attack against these disease problems. The National Program, developed by the National Heart and Lung Institute and its advisors, includes planning, research and development of prevention, education and control programs of relevance to the community. The Program has the following goals:

- To Promote Health
- To Prevent Disease
- To Treat Disease
- To Restore Health.

We have developed the Program with these goals in mind. It is scheduled to become activated in stages as resources become available. The Program calls for periodic reassessment of priorities and represents a dynamic and flexible approach responsive to the needs of our nation and the new opportunities opened up by scientific advances.

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I. INTRODUCTION

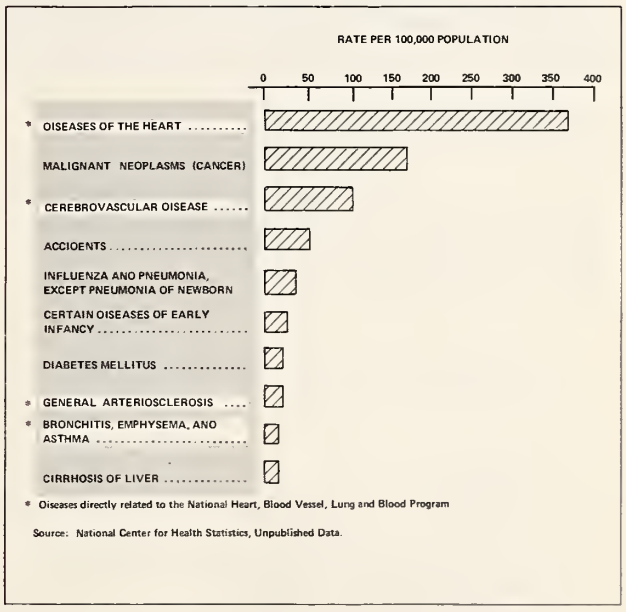
The National Heart, Blood Vessel, Lung and Blood Program presented in this Summary is focused on four major problem areas:

- Heart and Blood Vessel Diseases
- Lung Diseases
- Blood Diseases
- Blood Resources.

Heart, blood vessel, lung and blood diseases constitute the most important public health problem confronting the American people today. This statement is supported by all the common indices of public health impact such as the number of people affected, number of deaths, days of bed disability, hospital days, days lost from work, and economic costs of disease. Collectively, these diseases affect more than 30 million Americans and are the number one cause of death and disability in the nation. The maintenance of adequate function of the heart, lungs and blood, which is essential to health and life, has become a pressing national problem when viewed against the massive personal, social and economic losses which continue to accrue from these diseases.

The leading cause of death by far, plus three others among the ten leading causes of death in the United States (Figure 1), fall within the scope of the above problems. Heart and blood vessel diseases alone account for more than one million deaths each year—a rate equivalent to an average of two deaths every minute. Approximately one quarter of these deaths occur in persons age 65 or less, the most productive years of a person's life. In close to 100,000 persons with heart and blood vessel disease, sudden unexpected death is the first and only evidence of heart disease. The number of days of bed disability in 1971 (Table 1) directly attributed to the above disease problems was approximately 210 million. The total economic drain on society due to problems related to these diseases has been estimated at more than $40 billion annually. These statistics give a sobering overview of the magnitude and importance of the problems being addressed by the National Heart, Blood Vessel, Lung and Blood Program.

Figure 1
LEADING CAUSES OF DEATH
UNITED STATES, 1969



Recognition of the magnitude of these problems resulted in enactment of the *National Heart, Blood Vessel, Lung, and Blood Act of 1972* (see Appendix A). The Act provides a mandate for attacking the identified problems and requires the Director of the National Heart and Lung Institute (NHLI), with the advice of the National Heart and Lung Advisory Council, to develop a program for a national attack on these diseases.

This Act set into motion an intensive, six-month planning effort, directed by the NHLI to formulate a five-year plan for a National Program to accelerate the

Table 1

RANKING OF DISEASES ACCORDING TO HEALTH IMPACT, UNITED STATES, 1971

DISEASE	DAYS OF BED DISABILITY		HOSPITAL DISCHARGES		HOSPITAL DAYS	
	RANK	DAYS*	RANK	NUMBER*	RANK	DAYS*
Influenza & pneumonia	1	206,241	-	-	-	-
Upper respiratory	2	164,840	2	1,311	11	3,444
**Heart disease	3	93,137	1	1,390	1	17,921
Arthritis	4	57,539	12	217	9	3,837
Mental Disorders	5	41,965	5	695	3	15,273
Fractures & Dislocations	6	35,625	3	1,249	2	17,097
Malignant Neoplasms (Cancer)	7	32,374	6	646	4	7,785
Impairments of back & spine	8	31,895	-	-	-	-
**Hypertensive without heart involvement	9	27,476	9	314	12	2,780
**Bronchitis	10	27,388	-	-	-	-
**Asthma	11	25,997	-	-	-	-
**Cerebrovascular disease	12	24,762	11	264	7	5,128
Paralysis	13	24,052	-	-	-	-
Diabetes	14	23,739	10	280	10	3,498
Impairments of lower extremities	15	20,986	-	-	-	-
Ulcer	16	17,569	8	492	6	5,245
**Emphysema	17	13,124	-	-	-	-
Hernia	18	11,948	4	726	8	4,835
Gall Bladder	19	11,892	7	530	5	5,922
Absence of extremities	20	7,347	-	-	-	-
Impairments of upper extremities	21	5,491	-	-	-	-

- Data not available
* In thousands
**Addressed by National Program
SOURCE: Unpublished Data from the National Center for Health Statistics

attack on heart, blood vessel, lung and blood diseases and blood resource problems. The details of the planning effort are presented in Appendix B. The objectives of this planning effort were to:

- Define the national problems in heart, blood vessel, lung and blood diseases and blood resources
- Assess the current state-of-the-art in these problem areas
- Identify new opportunities and approaches for present and future application
- Survey ongoing related programs in federal and nonfederal organizations
- Review and evaluate this information base and draw conclusions regarding national needs
- Develop recommendations for a National Program to solve these problems
- Develop a dynamic, flexible planning strategy
- Develop mechanisms for coordination of a National Program
- Develop an initial five-year plan for a National Program to accelerate the attack on heart, blood vessel, lung and blood diseases and blood resource problems.

To accomplish these objectives, the NHLI relied heavily upon the participation of many individuals from diverse groups who contributed their advice and commentary to the planning effort. These groups and representatives included:

- Approximately 300 Panel and Task Group participants representing universities, medical schools, hospitals and other parent institutions throughout the United States
- National Heart and Lung Advisory Council
- Interagency Technical Committee on Heart, Blood Vessel, Lung and Blood Diseases and Blood Resources
- Nonfederal and voluntary organizations with related programs.

These groups generated an extensive information base for the National Program. The NHLI carefully considered this information in formulating this five-year plan for a National Program.

The plan is presented here in the National Heart and Lung Institute Summary (Volume I). This volume defines the major disease problems addressed by the National Program; discusses the strategy, direction, implementation and evaluation of the Program; presents the role of the Institute in this Program; and estimates the resource allocations needed for implementation of the initial five-year NHLI Program Plan.

The information generated during the planning effort is contained in four accompanying volumes which provide a rich source of data that will be used throughout the future development of the National Program. These volumes are as follows:

Volume II. Report of the National Heart and Lung Advisory Council.

Volume III. Report of the Panel Chairmen.

Volume IV. Panel Reports.

Part I. Report of the Heart and Blood Vessel Diseases Panel.

Part II. Report of the Lung Diseases Panel.
Part III. Report of the Blood Diseases Panel.
Part IV. Report of the Blood Resources Panel.

Volume V. Program Analysis.

Part I. National Heart and Lung Institute.
Part II. National Institutes of Health (exclusive of the National Heart and Lung Institute).
Part III. Other Federal Agencies

—Department of Agriculture
—Atomic Energy Commission
—Department of Defense
—Environmental Protection Agency
—Food and Drug Administration
—Health Services and Mental Health Administration
—National Aeronautics and Space Administration
—National Science Foundation
—Social and Rehabilitation Service
—Social Security Administration
—Department of Transportation
—Veterans Administration.

This summary volume of the National Program is presented in nontechnical language, insofar as possible, in order to facilitate communication with interested laymen who may be unfamiliar with medical terminology.

II. THE PROBLEMS

There are many urgent problems in heart, blood vessel, lung and blood diseases and blood resources. This section defines only the major problem areas identified by the National Heart and Lung Institute and its advisors. The brief discussion for each problem area includes definition, relationship to other diseases and/or disorders, and impact and scope of the problem in our country. The section also highlights past accomplishments and future challenges related to these disease problems.

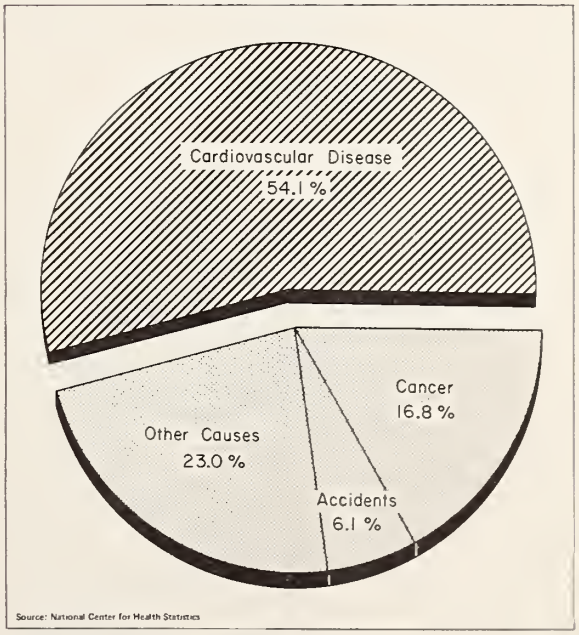
DEFINITION OF MAJOR PROBLEM AREAS

The four major problem areas covered by the National Heart, Blood Vessel, Lung and Blood Act are discussed separately in the following three sections: Heart and Blood Vessel Diseases, Lung Diseases, Blood Diseases and Blood Resources. As pointed out in the Report of the Panel Chairmen, there are many interrelationships among these problem areas. The Chairmen state: "Disordered biological functions seldom involve a single area. As examples, pulmonary embolism begins with thrombosis and involves the lung and its circulation as well as the heart. Effective delivery of oxygen to the tissue depends on the lung, the heart, the amount, type, and functional states of the hemoglobin, and the peripheral circulation."

HEART AND BLOOD VESSEL DISEASES

For more than fifty years, heart and blood vessel diseases have been the major cause of death in this country. They now account for 54 percent of all deaths annually (Figure 2). This is more than three times the death rate from cancer, the next highest cause. An estimated 28 million Americans have diseases of the heart and blood vessels, resulting in a large burden of acute and chronic illness and disability. Hence, there is reason for referring to heart and blood vessel diseases as the modern epidemic. Moreover, heart and blood vessel diseases cost the economy more than $30 billion per year in wages, lost productivity, and expenses for medical care.

Figure 2
DEATHS FROM ALL CAUSES
UNITED STATES, 1967



Nine major problem areas in heart and blood vessel diseases are defined below: Arteriosclerosis, Hypertension, Cerebrovascular Disease, Coronary Heart Disease, Peripheral Vascular Diseases, Arrhythmias, Heart Failure and Shock, Congenital and Rheumatic Heart Diseases, and Cardiomyopathy and Infections of the

Heart. Of these, arteriosclerosis and hypertension are considered the major cardiovascular disease problems in the United States. The causes of arteriosclerosis and most cases of hypertension are unknown.

Arteriosclerosis, or "hardening of the arteries," is responsible for 84 percent of the deaths from heart and blood vessel diseases. It is a chronic pathological change in the blood vessels and its most common form is atherosclerosis in which the inner lining of the arteries becomes rough, thick, hard and covered with plaques. Eventually, the inner diameter of the vessels decreases and blood flow in the diseased arteries diminishes or stops completely. Atherosclerosis begins early in life and is asymptomatic for years. Virtually all adult American males, and post-menopausal women, are afflicted to some degree. The disease manifests itself in many ways, but primarily as heart attacks, strokes and occlusive disease of the peripheral vessels. Therefore, if arteriosclerosis could be prevented, hundreds of thousands of lives might be prolonged. International statistics reveal a great variation in death rates for coronary heart disease. For instance, in Denmark, Norway, and Sweden, the death rate for men under the age of 55 is less than half that for the same age group in the United States. This difference indicates that the high death rates due to arteriosclerosis in the United States are neither necessary nor inevitable.

Hypertension, or high blood pressure, is one of the most commonly encountered forms of heart and blood vessel diseases, affecting an estimated 23 million adult Americans, or between 10 and 15 percent of the population. High blood pressure is the most important factor contributing to the development of strokes. It also accelerates the development of atherosclerosis in the coronary and peripheral vessels. Control of hypertension would, therefore, reduce the incidence of three major causes of death and disability: stroke, coronary heart disease and peripheral vascular disease. High blood pressure is easy to detect, but may exist for many years without symptoms. It can be controlled with presently available therapy. However, of the millions of Americans with this disease, one half are probably unaware that they have it, and of those who are aware, less than one half are receiving adequate therapy. Although hypertension is widely distributed among Americans, it has been found to be more common and severe among the black population.

Cerebrovascular Disease occurs when an artery supplying blood to the brain is blocked, ruptured, or injured. Cerebrovascular disease due to arteriosclerosis and especially due to hypertension is the basis for the great majority of strokes. The individual and public health burden of death, paralysis and brain damage is large. Of the 1.7 million adults who have this disease, 700,000 are partially or completely disabled. Stroke kills about 200,000 persons a year, more men than women, and at a greater rate among blacks than whites. Each year, some 530,000 patients are discharged from our hospitals with a diagnosis of stroke, and each year about 250,000 individuals, between the ages of 25 and 64, are crippled mentally or physically by a stroke. Many more lives could be saved and disabilities prevented if we had effective methods for prevention and treatment of arteriosclerosis and hypertension and if available treatment were more widely applied. It should be noted that, due to the recent advances in therapy for high blood pressure, there has been an appreciable long-term decrease in deaths from stroke.

Coronary Heart Disease refers to atherosclerosis in the arteries that supply the heart muscle. A heart attack is a manifestation of coronary heart disease and occurs when a coronary artery is blocked, preventing the blood from reaching the heart muscle. This produces death of the heart muscle, technically called myocardial infarction. Coronary heart disease is the major manifestation of atherosclerosis. It is the predominant form of heart disease in the adult American and causes 1.25 million heart attacks a year, and is responsible for chronic illness in 4 million Americans, 2.5 million below the age of 65. In 1969, coronary heart disease accounted for about 675,000 deaths in this country. It is the largest single cause of death from cardiovascular disease and is the leading cause of death in both men and women. Each year, approximately 130,000 persons in their most productive years (below age 65) die of coronary heart disease.

Coronary heart disease may also result in angina pectoris (a pain usually located in the chest and arm that is brought on by exercise, exposure to cold, and other factors), heart failure (impaired pumping performance of the heart leading to accumulation of fluid in the body and congestion in the lungs), disturbances of heart rhythm and sudden death. Each year, 400,000 deaths from coronary heart disease occur suddenly or before hospitalization. Half of these occur instantaneously and unwitnessed. Either heart disease or hypertension is evident in 300,000 of these cases, but in 100,000, sudden cardiac death is the first evidence of heart disease.

Peripheral Vascular Diseases are abnormalities that occur within arteries or veins. Atherosclerotic narrowing may result in inadequate blood flow through the

arteries. The veins may become dilated (varicosities) or inflamed and obstructed by blood clots (thrombophlebitis). These diseases may be painful and result in organ damage, skin ulcerations and gangrene. Peripheral vascular diseases are a significant cause of disability and illness. For example, peripheral vascular disease in the legs may affect one's ability to walk or run. Thrombosis in the veins may produce pulmonary embolism; i.e., clot fragments may be carried in the blood from their site of origin to the lungs. This in turn may result in shock and death. Leg vein thrombosis is the cause of more than 90 percent of pulmonary emboli which in turn are responsible for approximately 50,000 deaths a year in this country. About 265,000 patients are discharged from our hospitals each year with a primary diagnosis of peripheral vascular disease.

Arrhythmias, or abnormal heart rhythms, occur with many forms of heart disease and result from an alteration in the normal transmission of electrical impulses within the heart. They may also occur without recognizable disease. Many rhythm disturbances have minor influence upon life expectancy and cause little disability, others cause serious symptoms, and some are almost instantaneously fatal. For example, arrhythmias kill more than half of the patients with coronary heart disease and are a major problem in patients with rheumatic heart disease.

Heart Failure and Shock represent major causes of death and may be the end result of many different diseases. Heart failure occurs when the heart has been damaged so extensively that its ability to pump blood is impaired and it can no longer meet the needs of the body. In its chronic form, it is often associated with shortness of breath, accumulation of fluids and swelling of the legs. Shock is also a secondary phenomenon characterized by an inability of the heart and peripheral circulation to maintain adequate blood pressure or blood perfusion. Left untreated, it rapidly leads to irreversible damage to the tissues, and to death. Shock can be a complication of many disorders such as heart attacks, hemorrhage, or burns and stroke.

Heart failure and shock are the primary causes of in-hospital deaths from heart attack and most other types of heart disease, thus accounting for over a quarter million deaths annually. In addition, chronic heart failure may follow a heart attack or result from high blood pressure or other heart diseases. Over two million Americans have chronic heart failure, and each year the total cost of their hospitalization exceeds $500 million. In the majority, symptoms can be relieved by drugs.

Congenital and Rheumatic Heart Diseases are important diseases of children. Congenital heart disease occurs when the heart or major blood vessels near the heart fail to mature normally before birth. About eight out of every 1,000 children are born with this disease, and half of them do not survive until their first birthday. The causes of congenital heart diseases are generally unknown. Less than 3 percent are known to be related to a particular event or disorder occurring during pregnancy, such as rubella infection or the use of certain drugs, such as thalidomide. Rheumatic fever and rheumatic heart disease were once considered leading causes of childhood illnesses. They can now be prevented. Rheumatic fever is almost always preceded by a streptococcal infection and may lead to damage of the heart valves, thus causing rheumatic heart disease. Rheumatic fever afflicts about 100,000 school children. Both congenital and rheumatic heart diseases cause substantial impairment of health in children, and in adults in their most productive years. They annually cause over 8,000 and 15,000 deaths, respectively, in the United States. The cost of physician care alone for patients with rheumatic fever and rheumatic heart disease was about $28 million in 1969.

Cardiomyopathy and Infections of the Heart are diseases of the heart muscle and its linings. These diseases cause enlargement of the heart, heart failure, irregularities of the heart rhythm, and occasionally sudden death. They are the result of a variety of factors. Known factors include toxic substances, viral infections, alcohol, immunological phenomena, nutritional deficiencies, muscular dystrophy, and a number of rare diseases. The condition may be acute or chronic and progressive. Rapidly fatal disease may be associated with heart failure, disturbances of rhythm and sudden death. Infections may affect the heart muscle (myocarditis), its interior wall (endocarditis), or its exterior surface (pericarditis). Cardiomyopathies, myocarditis, endocarditis, and pericarditis are increasing in frequency. However, quantitative information concerning the prevalence of these diseases is not available because we still lack specific diagnostic criteria and laboratory tests.

LUNG DISEASES

The National Heart, Blood Vessel, Lung and Blood Program encompasses respiratory diseases exclusive of cancer of the lung, upper respiratory infections and pulmonary tuberculosis.

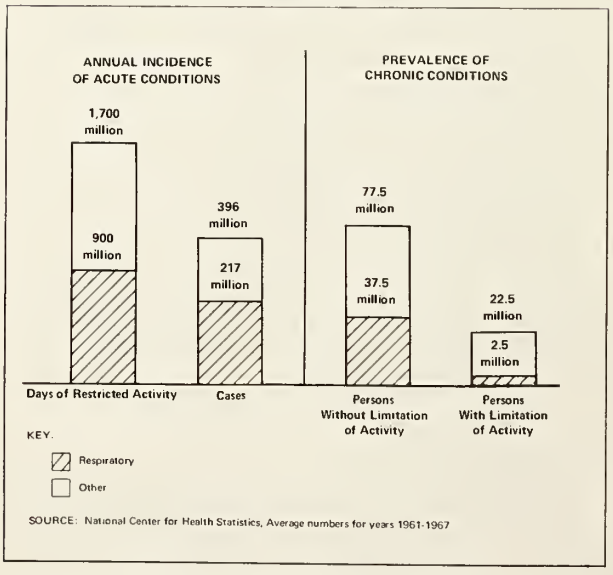
Respiratory diseases that represent national health problems include chronic obstructive pulmonary dis-

eases (COPD), acute respiratory distress syndromes (RDS), and interstitial lung diseases. The economic cost of these diseases has been estimated at $6.3 billion per year.

Lung diseases afflict both the young and the old. In the newborn, the most common cause of death is the respiratory distress syndrome which affects between 50,000 and 100,000 babies in the United States each year, about half of whom die. RDS is implicated in the development of adult respiratory diseases as well. Interstitial lung diseases are a major cause of lung problems in the young adult, and may cause COPD. Of the adult respiratory diseases, emphysema and chronic bronchitis are the major causes of death. An estimated 10 million Americans are currently affected by these diseases, together with asthma. Emphysema and chronic bronchitis represent a particularly pressing health problem since the death rate and prevalence of these conditions have been increasing at an alarming rate over the past 15 years.

As a disabling disease, emphysema is second only to heart disease. The illness and disability caused by respiratory diseases are summarized in Figure 3.

Figure 3
ILLNESS AND DISABILITY FROM RESPIRATORY DISEASES IN THE UNITED STATES



Four major lung disease problems are defined below: Pediatric Pulmonary Diseases, Emphysema and Chronic Bronchitis, Fibrotic and Immunologic Lung Diseases and Respiratory Failure.

Pediatric Pulmonary Diseases present health problems of national dimensions. Hyaline membrane disease (respiratory distress syndrome of the newborn), cystic fibrosis (an inherited disease of abnormal mucus secretion), and bronchiolitis (acute airway obstruction in young children) are among the most important disorders of childhood that involve the lung and the airways. About 40,000 babies are born each year with hyaline membrane disease. More than half of these will die unless given prompt treatment, presently unavailable except in a few specialized facilities.

Cystic fibrosis occurs in about one of every 2,000 live births and approximately 5 percent of the general population in the United States carries the gene for this disorder. Cystic fibrosis is one of the main causes of chronic illness in children and young adults and accounts for most of the deaths from pulmonary disease in the pediatric age group. Bronchiolitis is a common pediatric disorder, but data are not available on its incidence.

Emphysema and Chronic Bronchitis are among the major causes of mortality and illness from pulmonary diseases. Emphysema is a disease in which the thin walls in the alveoli (air sacs) lose their elasticity and tear. Chronic bronchitis refers to a persistent inflammation of the lungs characterized by recurrent coughing and excess mucus in the airways. These diseases may be associated with certain risk factors, such as cigarette smoking, and in some cases with genetic determinants (e.g., deficiency of alpha$_1$-antitrypsin enzyme). Emphysema is a leading cause of death in this country and an even greater cause of disability. Data from 1967 indicate that chronic bronchitis and emphysema account for half of the total 181,000 man-years lost due to lung diseases. The death rate for chronic bronchitis increased by 80 percent between 1958 and 1967. The death rate for emphysema increased by 172 percent in the same period to a level of 10.6 per 100,000 population.

Fibrotic and Immunologic Lung Diseases are induced by many disease factors. Fibrotic responses (proliferation of connective tissue or scar formation) and immunologic responses are characteristic of a variety of lung diseases. Among the factors that may induce these responses are exposure to substances such as coal dust, silica, and asbestos in the environment; viral and bacterial infections; diseases of the connective tissue such as rheumatoid arthritis, lupus, and scleroderma; radiation damage; and exposure to substances like molds and dust that initiate hypersensitivity reactions. Diseases characterized by pulmonary fibrosis and/or

immunologic reactions include pneumoconiosis, sarcoidosis, diffuse hypersensitivity pneumonitis, Farmer's lung and bronchial asthma. This group of lung diseases is a major national health problem, second in magnitude among lung diseases only to emphysema and chronic bronchitis.

Statistical data on fibrotic lung diseases are inadequate because these diseases are difficult to diagnose and poorly reported. However, their national health impact is far greater than is generally appreciated. For example, sarcoidosis is about 12 to 15 times more common among blacks than among whites in this country, and now outranks tuberculosis as a cause of disability from pulmonary insufficiency in black populations. It is also more common in women.

Among immunologic lung diseases, asthma is the most common, affecting about 8.6 million persons in this country (approximately 4 percent of the population). It is responsible for 5 percent of all chronic disabilities and causes an annual loss of about 7 million work-days. Other immunologic lung diseases are associated with specific occupations where exposure to organic dusts or molds is high; for example, Farmer's lung in the north central states, Bagassosis among sugar cane workers in the south, and hypersensitivity pneumonitis from organisms growing in humidifiers and air conditioners. While none of these diseases is very common in the general population, their importance stems from their high incidence in particular environments.

Respiratory Failure is a complication of many nonpulmonary diseases. Acute respiratory distress syndromes have been recognized as such only recently. For these two reasons, data on incidence are not available. A conservative estimate is that 150,000 adult cases of acute respiratory distress syndrome occur each year with a mortality rate of 40 percent. These figures do not include failure due to chronic pulmonary disease, (see Emphysema and Chronic Bronchitis), nor do they adequately reflect the true incidence because so many cases are unreported.

BLOOD DISEASES AND BLOOD RESOURCES

Problems of the blood are intimately related to cardiovascular and pulmonary diseases. Blood is a vital part of the circulatory system since it is the vehicle by which oxygen, nutrients, and other body chemicals are carried through the blood vessels to every part of the body, to be exchanged for carbon dioxide, waste products and chemicals which, in turn, need to be transported away from the tissues to other body organs, either for excretion from the body or for use in the life processes.

Three groups of blood problems are defined below: Bleeding and Clotting Disorders, Sickle Cell Disease and Related Disorders of the Red Blood Cell, and Blood Resources.

Bleeding and Clotting Disorders are closely interrelated. Both represent failures in maintaining the blood in an optimal state within the blood vessels. On one hand, failure means bleeding (hemorrhage) into surrounding tissues or outside the body. On the other hand, failure means inappropriate clotting (thrombosis) of the blood within the vessels. Clotting in the arteries deprives a part of the body of its blood supply; clotting in the veins impedes the return of blood to the heart. When excessive clotting affects small blood vessels and capillaries (collectively termed the microcirculation), tissues and cells cannot function well because they are deprived of essential oxygen, energy, regulating hormones and building blocks, and noxious waste products cannot be removed effectively.

The particular portion of the body's defense mechanisms responsible for maintaining the blood in an optimal fluid state is termed the hemostatic system. Excessive bleeding can result from an abnormality or deficiency, acquired or inherited, of any of the elements in the hemostatic system. Bleeding into organs and tissues may impair or destroy their function and uncontrolled, external blood loss may result in death.

The consequences of abnormal clotting depend on the organ or region of the body in which it occurs. In vessels of the heart, brain, lung or other vital organs, the result can be catastrophic; in less vital areas, the effects may be mild and transitory. With time, the clot-dissolving mechanism restores the integrity of the circulation. However, the speed of this process is insufficient in the case of vital organs where even a very brief deprivation of blood supply results in irretrievable loss of function or death of tissue.

The impact of the clotting and bleeding disorders is considerable. Arterial thrombosis causes or complicates a great variety of diseases in all parts of the body; for

example, thrombosis involving the vessels of the kidney contributes to kidney failure, and arterial thrombosis and cerebral hemorrhage play major roles in stroke.

Thrombosis in the veins may produce pulmonary embolism; that is, clot fragments may be carried in the blood from their site of origin to the lungs. About 300,000 persons are hospitalized annually and more than 50,000 die with pulmonary embolism. Clotting in the venous circulation complicates many illnesses and surgical procedures. Autopsy studies show evidence of venous thrombosis in about 50 percent of cases examined, regardless of cause of death.

The microcirculation is a very important component of the circulation system. It conveys to the cells of the body the substances needed for their metabolism and regulation, and carries away their products so that the internal environment is maintained in a manner which allows the cells to survive and perform their interrelated tasks. Bleeding and clotting in the microcirculation are contributory or primary mechanisms in hypertension, stroke, diabetes, infectious and inflammatory disease, autoimmune disease, host-graft rejection, cancer, sickle cell anemia, drug toxicity, mismatched blood transfusion, liver disease, and nephritis. The impact is vast even if it cannot be expressed statistically.

Thrombosis induced by contact of the blood with foreign surfaces remains the major unsolved problem in the development of artificial organs, prosthetic vessels or devices that temporarily assist the circulation.

Excessive blood loss due to inadequate or disturbed function of a component of the hemostatic mechanism is a major cause of death and morbidity in a variety of circumstances such as after severe injury, after surgery, in leukemia, and in cirrhosis of the liver. The threat of hemorrhage limits the aggressive management of some forms of cancer.

The hemophilias are sex-linked, hereditary diseases occurring almost exclusively in males. Although the known hemophilic population of this country is only about 25,000, hemophilia constitutes a major national health problem for two reasons. First, treatment must be continued throughout the lifetime of the patient at enormous cost (the current yearly cost to replace the missing clotting factor alone is estimated to be in excess of $6,000 per patient, or more than $120 million for the 80 percent of hemophiliacs who can benefit from this factor). Second, treatment of the disease presents one of the largest single demands upon the nation's blood resources.

Sickle Cell Disease and Related Disorders of the Red Blood Cell include sickle cell anemia, Cooley's anemia and defects affecting the red blood cell membrane or enzyme systems.

Sickle cell anemia, Cooley's anemia and certain defects affecting the red blood cell membrane or enzyme systems are all genetically determined and are presently incurable, although they may be controlled to varying degrees. These disorders lead to premature destruction of the red cells in the circulation. Anemia results because the bone marrow is unable to produce sufficient numbers of new cells to keep up with the rate of destruction.

Approximately two million individuals, primarily black, carry the sickle cell trait. They are healthy, but if two carriers marry, each of their children has a one in four chance of having sickle cell anemia, a painful and debilitating disorder. About one in 400 black babies in this country is born with sickle cell anemia, and somewhat less than 50,000 individuals suffer the painful episodes known as "crises."

The cost of caring for a patient with sickle cell disease may approach $2,500 to $5,000 a year. The loss of time from school, from jobs and the resultant psychological and educational problems, make this disorder one of high social and economic importance.

Cooley's anemia results from defective production of one of the subunits of the hemoglobin molecule, leading to rapid destruction of the red cells. It occurs in perhaps 5,000 Americans, largely of Mediterranean ancestry. Its victims suffer profound anemia and require repeated blood transfusions for survival. As with the sickle cell trait, carriers do not have symptoms, but offspring may be affected.

Defects in red cell membranes and red cell enzymes also produce anemia. Such defects are relatively rare, although one, called glucose-6-phosphate dehydrogenase deficiency (G6PD), occurs in about 10 percent of black males and less frequently in males of Mediterranean ancestry. Most of these individuals are

healthy, but they are sensitive to a variety of commonly used drugs and may develop anemia if they take them. They also develop anemia with certain illnesses.

Blood Resources for the nation need to be available in an adequate supply. High quality blood and blood products is essential for the effective treatment of many diseases. Whole blood is made up of cellular elements dispersed in a fluid medium called plasma. The cells consist of red cells to deliver oxygen, platelets to stop bleeding, and white cells to fight infection. Plasma contains such useful products as albumin, immunoglobulins, and clotting factors.

To give the patient enough of what he needs and when he needs it requires recruiting the donor, collecting his blood, separating it into its components, detecting and eliminating disease-causing agents, matching the components for compatibility, and administering it to the patient in a fail-safe fashion.

In the United States, an assemblage of organizations (which might be referred to as the blood service complex) acquires, processes, stores, delivers and administers blood and a variety of blood products. This complex has an estimated gross annual income exceeding $500 million. It collects about nine million pints of blood per year for transfusion. About 25 percent of this blood is never transfused and much of this portion is wasted.

Whole blood is mostly collected by the blood-banking sector of the complex. In addition, the pharmaceutical industry, which comprises the other major sector, collects about 1.7 million liters of plasma each year, mainly for the preparation of plasma fractions (about one liter of plasma is present in five units of whole blood).

Transfusion is not without dangers, one of which is the possibility of hepatitis. Approximately 10 to 15 percent of the whole blood collected by the blood-banking sector is obtained from commercial donors. This blood accounts for about a quarter to a half of the incidence of post-transfusion hepatitis. While nationwide reporting of hepatitis of any origin or type is unreliable, it is estimated that each year post-transfusion hepatitis accounts for 850 deaths, 17,000 episodes of illness which are often incapacitating for weeks to months, and another 100,000 infections without symptoms. If we consider only the patients who become ill, their average hospital stay is 28 days. The dollar cost to the nation approximates $86 million per year; costs in terms of human suffering are immeasurable.

PAST ACCOMPLISHMENTS AND FUTURE CHALLENGES

Although the problems appear overwhelming, they would loom as much greater threats to the individual and have a far greater impact on society today were it not for the accomplishments in biomedical research made during the past 25 years. This section highlights some of the past accomplishments in these problem areas and presents challenges of the future as a background for developing a National Program.

In the heart and blood vessel diseases, we have identified the contributory risk factors for arteriosclerosis, and by various techniques can detect and diagnose many cardiovascular diseases. We know that arteriosclerosis leads to heart attacks and strokes. We know how to correct surgically arteriosclerotic obstructions in the arteries and how to use drugs to treat patients with high blood pressure and thereby reduce the incidence of stroke and heart failure. We can identify and correct most congenital heart defects, and can prevent rheumatic fever and rheumatic heart disease by penicillin treatment of throat infections. Heart-lung machines have been developed as life-support mechanisms for use in surgery and we can use electronic pacemakers to regulate heart rhythms.

In the lung diseases, we are able to determine functional defects of the lung by physiological tests and have largely brought under control two major killers of the past—pneumonia and tuberculosis.

In the blood diseases, we know the causes of bleeding in hemophilia patients and are able to prescribe treatment to control it. We know that hemophilia, sickle cell disease and Cooley's anemia are inherited blood disorders.

Still, many questions remain unresolved, for the causes of many of these diseases are still unknown and our

ability to promote health, prevent the onset of disease, treat disease, and restore individuals to vigorous health needs to be enhanced. For example, we do not know what causes most forms of high blood pressure, what mechanisms cause hardening of the arteries, or most of the factors that cause congenital heart disease. Identification of risk factors is indeed a proud accomplishment; however, proving through clinical trials that removal of these risk factors will decrease cardiac risk is indeed a major challenge to the future. If risk can be changed through treatment then indeed coronary heart disease and atherosclerosis can be prevented or at least controlled. We do not yet understand the cellular biology of lung tissue and we have yet to design adequate treatment for acute respiratory failure. And, we need to develop and test better methods of screening for, and control of, sickle cell disease and Cooley's anemia.

Besides these unresolved questions, and there are many others, which have been with us for a long time, there are other, relatively new areas of concern that confront us. The chronic obstructive pulmonary diseases, especially emphysema and chronic bronchitis which are the two most common and serious of these disorders, are increasing in our population. These two diseases restrict the activities of hundreds of thousands of Americans and promise to affect many others as our air pollution problems worsen. Diseases from dust inhalation, especially pneumoconiosis, are serious health problems which may lead to extreme disability and even death. And, persons who work with asbestos, quartz, coal, iron, cotton and sugar cane, may suffer from environmental irritants and be predisposed to developing chronic bronchitis and emphysema.

Similarly, the ever hastening pace of modern society is manifested in increasing rates of stress which may be a contributing factor in the development of heart attacks. And, the extent of sickle cell disease and high blood pressure among American blacks has only recently become known.

Fortunately, today, there is a growing awareness of the magnitude and urgency of these problems. The research community is cognizant of the research advances that have been made and the directions projected. In accordance with the design of a National Program, we also need to bring this knowledge to the general public. The National Program presented below is addressed to both the medical and scientific communities and the general public to participate jointly in the attack against heart and blood vessel, lung and blood diseases.

III. PLANNING FOR A NATIONAL PROGRAM

A growing emphasis on planning has taken place in health programs during the past few years as we have become increasingly aware of the magnitude of some of these disease problems in an environment constrained by finite resources. The United States Senate, reflecting this emphasis, has formally called for (in Report No. 92-894) comprehensive planning in biomedical research.

The development of any comprehensive plan is rarely a simple projection of projects and approaches to well-defined problems to achieve specific goals and objectives. This is especially true in biomedical research where "approaches" exist which cannot be planned. However, this does not mean that planning is inappropriate or that unanticipated "approaches" cannot be planned for. It does mean that any plan for biomedical research should have the flexibility and mechanisms to promote research which will lead to important innovations and, at the same time, be responsive to growing demands for accountability by the public community. Thus, the plan must provide for a whole spectrum of approaches ranging from highly structured interdisciplinary programs at one end to independent investigators initiating their own projects at the other end. We realize that maximum flexibility for totally independent scientific investigation, without regard to the public's demands for solutions to specific disease problems, could lead to no real plan at all, while maximum responsiveness to demands for accountability could lead to a rigid, highly structured plan, which would minimize the chances of important new discoveries.

The National Science Foundation Division of Science Resources, in a recent series of studies of the innovation process, has illustrated the diverse ways by which research and development activities support each other in the innovative process (*Science, Technology, and Innovation,* NSF-C667) and pointed out ways in which innovation can be promoted. These studies conclude that innovation cannot be completely controlled or programmed and recommend that management, in trying to promote innovation, permit and encourage the opportunity to act upon ideas that fall outside the established or recognized pattern. However, these analyses also reveal that management can help promote innovation, primarily in two ways: (1) by providing adequate financial support which permits innovative projects to proceed and which generates confidence that aids the innovative process, and (2) by promoting interdisciplinary studies to accelerate the innovative process.

In striving to meet the challenge, a plan for a National Program is emerging which is not static, as implied by the term "blueprint," but rather a flexible, dynamic, continuous evolving process—a national planning process of projection, evaluation and modification. This section describes this process and includes discussions of the need for a plan, the evolving program strategy, and methods of program coordination, implementation, review and evaluation.

THE NEED FOR A PLAN

The need for a plan to launch a national program of attack on the problems of heart and blood vessel, lung and blood diseases has evolved from the recognition that isolated approaches are no longer appropriate to the growing magnitude of these public health problems. A major national program for marshalling

the resources of this country to provide better health for its citizens requires a vehicle for:

- Delineating overall program strategies
- Coordinating and implementing the program
- Communicating program needs and progress to the President and the Congress, to the general public and to the scientific community.

The plan for a National Program emerging from the current NHLI planning effort is that vehicle for the National Heart, Blood Vessel, Lung and Blood Program. The mandate for developing this plan is both comprehensive and far-reaching and was provided in Public Law 92-423, dated September 19, 1972 (Appendix A). The major thrusts of this Legislation are:

- The Director of the National Heart and Lung Institute must, with advice of the National Heart and Lung Advisory Council, prepare a plan within 180 days of the effective date of the Act.
- This plan is to be transmitted to Congress.
- The Program must be implemented in accordance with the plan.
- The plan must be reviewed annually, updated for the next five years and reported to the President for transmittal to the Congress.
- The plan must be coordinated with other research institutes of the National Institutes of Health.
- The plan must be coordinated with other federal agencies through an Interagency Technical Committee.
- The plan is to be coordinated with nonfederal organizations including state and local as well as nonprofit private agencies.
- Not less than 15 percent of the fiscal resources shall be applied toward solving the problems of blood diseases.
- Not less than 15 percent of the fiscal resources shall be applied toward solving the problems of lung diseases.
- The Director of the National Heart and Lung Institute may provide for the development of National Research and Demonstration Centers for Heart, Blood Vessel, Lung and Blood Diseases.
- The Director, under policies established by the Director of the National Institutes of Health and after consultation with the National Heart and Lung Advisory Council, shall establish heart, blood vessel, lung and blood disease prevention programs.

In response to this legislative charge, a program has been formulated which is national in character, flexible in form and responsive to the growing magnitude of heart, blood vessel, lung and blood disease problems. This program strategy is outlined in the next section.

PROGRAM STRATEGY

The long-range goal of any National Program addressed to a public health problem is to improve the health of the American people. The formulation of a sound program strategy for attacking major public health problems such as heart, blood vessel, lung and blood diseases by an accelerated national effort can be hindered by high expectations for immediate results and achievement of goals according to a predetermined schedule. In such an environment where immediate payoffs are anticipated, there is the inherent danger of formulating strategies which appear to fulfill these high expectations, but, when implemented, actually become counterproductive.

The above issue was of fundamental importance in the Institute's deliberations which led to the formulation of the program strategy for the National Heart, Blood Vessel, Lung and Blood Program. The key decision and underlying premise which resulted from these deliberations was the firm conviction that a program strategy must evolve naturally from the information exchange and cooperative decisionmaking of groups which would be affected by such a plan. The development of the plan for the National Program was thus initiated without a preconceived, detailed planning framework. As a result, the plan has evolved and will continue to evolve as a natural outgrowth of the cooperative

application of basic planning principles by many diverse groups. These groups will provide continuous input to the National Program; they represent many different points of view as follows:

- American public — program goals and achievements
- Biomedical research community — program implementation
- Medical community — application of program results to improve health
- The President and the Congress — national policy, accountability
- National Heart and Lung Institute — program planning, management and implementation
- Other federal agencies — related programs
- Nonfederal organizations — related programs.

Although the program strategy has been allowed to evolve naturally, we recognize the need for a starting point and a rational mechanism for this evolvement. Thus, the program strategy, which has evolved from the considered interests and participation of these groups, has as its rational underpinnings the fundamental truth that solutions to disease problems can only be achieved through the ordered sequence of:

- Acquisition of fundamental knowledge
- Test and evaluation of existing knowledge
- Application of existing knowledge.

These activities are linked inextricably one to the other—application must be preceded by test and evaluation of existing knowledge, which, in turn, feeds on a continuing supply of new fundamental knowledge. The program strategy described here is a balanced one which seeks to emphasize those activities in the above sequence which are likely to have the greatest impact on a specific disease problem both in the short and long term. A significant impact can be made on some disease problems today by the immediate application of existing knowledge. We know, for example, how to control high blood pressure through regular application of tested drug therapy, even though the causes of most high blood pressure are unknown. However, approximately one-half of the 23 million persons in the United States with high blood pressure are not aware that they have it, and those who are aware, are reluctant to follow the lifetime regimen of drug therapy required to control high blood pressure. Thus, immediate application of existing knowledge for control of high blood pressure becomes a problem of information and education of the public which can be solved by highly specific and structured approaches.

At the opposite extreme are major disease problems such as atherosclerosis, the underlying cause of most heart attacks, for which the basic causes are unknown, and for which no effective means exist for treatment and control. Solutions to such disease problems must await the accumulation of a sufficient reservoir of new knowledge before the basic mechanisms are understood and new methods of detection, diagnosis and treatment can be devised. This reservoir can best be filled by the application of imaginative, innovative scientific minds working in a more loosely structured environment.

The program strategy evolving thus calls for a continuous spectrum of planning approaches ranging from highly specific, tightly controlled approaches at one extreme to relatively unstructured approaches at the other extreme. The degree of rigidity for approaches used for a specific problem will evolve as a natural consequence of the current state of knowledge for that problem. In this way, we hope to implement a program strategy which achieves a balanced plan of attack in which optimal approaches are used for each problem. The program strategy, summarized concisely, is to marshal national resources for promoting and restoring health, and for preventing and treating disease more effectively by:

- Initiating an ordered sequence of coordinated program activities from the acquisition of new knowledge to demonstration and control programs in the health care setting of the community
- Providing adequate program evaluation before the application of existing knowledge to health care delivery systems
- Evaluating the impact of implemented programs on the health of the people.

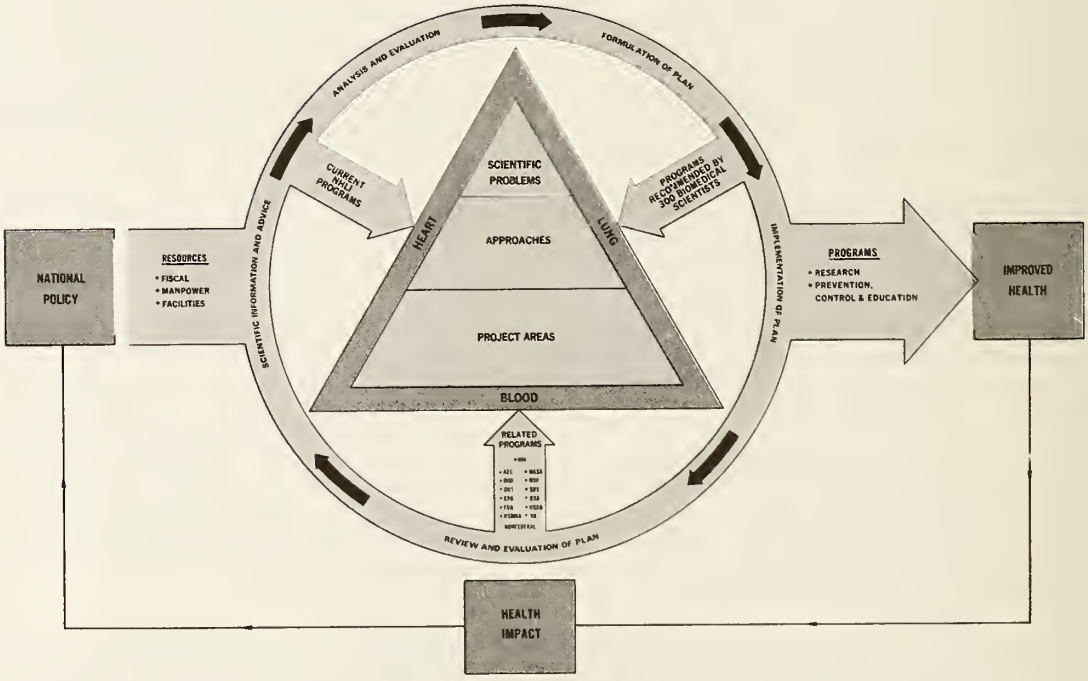
The cutting edge of the national attack will be a coordinated biomedical research program designed to achieve orderly and simultaneous progress along two interrelated program directions:

- Research Programs
- Prevention, Control and Education Programs.

It is the Institute's intention that the plan for a National Program which has been initiated remain a dynamic one, that it represent a credible plan of action now, and that it remain valid and credible as it evolves in the future. The overall program strategy for the National Heart, Blood Vessel, Lung and Blood Program is depicted by the diagram in Figure 4.

Figure 4

NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM STRATEGY



PROGRAM COORDINATION AND IMPLEMENTATION

Maintaining program balance with respect to a given problem area requires a thorough assessment of the current state of our knowledge in that problem area. The identification of these problem areas, assessment of existing knowledge and development of approaches for solving the problems have been the major emphasis of the current planning effort and represent the first step toward implementing the program strategy outlined above. Approximately 2000 project areas in 400 approaches to 39 problem areas were identified by the 300 biomedical specialists working in the planning effort described in Appendix B.

The number of organizations contributing to research activities related to the Program is extensive, and is composed of four major segments:

- National Heart and Lung Institute

- Other institutes and divisions of the National Institutes of Health
- Federal agencies exclusive of the National Institutes of Health
- Voluntary organizations.

An Interagency Technical Committee (Figure 5) has been formed to coordinate federal agency activities related to all aspects of the disease problems. Membership of the Committee includes representatives from the National Institutes of Health, Department of Agriculture, Atomic Energy Commission, Department of Defense, Environmental Protection Agency, Food and Drug Administration, Health Services and Mental Health Administration, National Aeronautics and Space Administration, National Science Foundation, Social and Rehabilitation Service, Social Security Administration, Department of Transportation, and Veterans Administration. The Interagency Technical Committee has already met several times and has cooperated in the establishment of baseline data (see Volume V, Part III) which will serve as a framework for its continuing role in the coordination of relevant federal activities. A survey was conducted of related programs currently ongoing at the NHLI, other divisions and bureaus of the National Institutes of Health and 12 other federal agencies for the 39 problem areas defined by the Panels.

The survey of programs supported by the NHLI and by agencies represented on the Interagency Technical Committee yielded approximately 3500 project areas of related research programs. This information base of current programs must be extensively analyzed and evaluated before it can be fully integrated into the National Program, and this effort is currently underway.

Thirteen organizational components of the National Institutes of Health (in addition to the NHLI) contribute significantly to the solution of the disease problems addressed by the Program; 12 other federal agencies are engaged in research, clinical and support services related to these problems; and 24 voluntary organizations have been identified which conduct or sponsor relevant research.

In identified related activities alone, the four major segments (the NHLI, other institutes and divisions of the National Institutes of Health, federal agencies exclusive of the National Institutes of Health, and voluntary organizations) conducted and sponsored more than $316 million in research related to heart, blood vessel, lung and blood diseases and blood resources in FY 1972 (see Parts I-III of Volume V for detailed explanation). Of the $316 million, approximately $198 million is related to heart and blood vessel diseases; $57 million to lung diseases; $35 million to blood diseases; and $27 million to blood resources and transplantation. The currently available information on these relative contributions is fully presented in Volume V and summarized here in Tables 2, 3, 4 and 5.

An effort will be made to consolidate and update this information base to:

- Provide information and education to the public and the medical profession
- Provide scientific and technical information concerning new leads
- Provide an important basis for developing new programs and for directing the National Program.

The overall coordination and implementation of the National Program, viewed from an institutional perspective, is a management problem of how to translate national resources into effective programs of action. The management system envisaged for the overall coordination and implementation of the National Program is illustrated in Figure 6. This system is based on information generated during the planning effort, with key emphasis on the following:

- Interagency coordination
- The ordered sequence of program activities from acquisition of new knowledge to health care delivery in the community
- The importance of adequate program evaluation before the implementation of health care delivery programs
- The importance of evaluating the impact of implemented programs on the health of the people
- The dissemination of information and education to the public and medical professionals.

Figure 5

INTERAGENCY TECHNICAL COMMITTEE: NATIONAL INSTITUTES OF HEALTH

NIAID
The NIAID conducts and sponsors research on: microbiological and immunological involvement in cardiovascular and pulmonary function and disease, including rheumatic fever, endocarditis, glomerulonephritis, emphysema, nonallergic asthma and sarcoidosis; immunohematology; and immunosuppression in organ and tissue transplantation and lung infections.

NIAMDD
The NIAMDD conducts and sponsors research on: hematological diseases including anemias and thalassemias; connective tissue diseases of heart and blood vessels; lipids and lipoproteins; fluid and electrolyte balance; metabolism and nutrition and life cycle of blood elements; and cystic fibrosis and pulmonary alveolar proteinosis.

NCI
The NCI conducts and sponsors research on: tumors affecting coagulation mechanisms or cardiovascular and pulmonary regulation; transplantation; and blood resources fractionation, preservation and utilization.

NIDR
The NIDR conducts and administers research on: oral microvasculature; tissue compatibility; properties of biomaterials; collagen synthesis and degradation; immunological mechanisms; and transplantation genetics.

NIEHS
The NIEHS conducts and sponsors research on: the effects of agents at low concentrations acting over long periods; multiple agent synergisms; the modifying effects of variable physical and biological states within man on susceptibility to and course of disease induced by environmental agents; and long-term epidemiological studies of populations with unusual environmental experiences or unique morbidity and mortality experiences.

NEI
The NEI conducts and sponsors research related to: retinal vascular metabolism and circulation; ocular vascular dynamics; platelet aggregation in retinopathies; and corneal vascularization and preservation.

NIGMS
The NIGMS conducts and sponsors research on: biochemistry and biophysics of the cardiovascular system, the pulmonary system, and blood and its components; engineering of cardiovascular assist and repair devices; sociological aspects of heart and pulmonary disease; anesthesia, trauma, shock, and surgery for correction of cardiopulmonary disorders.

NICHD
The NICHD conducts and sponsors research on: cardiopulmonary involvement in fetal development and pregnancy, including toxemia; cardiovascular and respiratory diseases of the newborn(hyaline membrane disease); rheumatic heart disease, congenital defects and cardiomyopathies; cardiovascular complications in the perinatal period; hematologic disorders; and renal development of function.

NINDS
The NINDS conducts and sponsors research on cerebrovascular disorders (stroke) and neurological effects on the cardiovascular and pulmonary systems including hypertension and arrhythmia.

FIC
The FIC is responsible for the administration of Scientific Activities Overseas including the NIH Special Foreign Currency (P.L. 480) Program, Conferences and Seminars, International Fellowships, and Scholars in Residence Programs.

BHME
The BHME supports and administers training and education programs for health professionals and paraprofessionals.

NLM
The NLM conducts and supports the development of: publications and information retrieval related to cardiovascular, pulmonary and blood diseases and blood resources; and biomedical computer and communications systems to assist in research, medical education and health care delivery.

DRR
The DRR provides support to biomedical research institutions for noncategorical resources including: clinical research centers support; biotechnology resources; animal models; and general research support for multicategorical programs.

LEGEND:

NIAID - National Institute of Allergy and Infectious Diseases
NIAMDD - National Institute of Arthritis, Metabolism and Digestive Diseases
NCI - National Cancer Institute
NIDR - National Institute of Dental Research
NIEHS - National Institute of Environmental Health Sciences
NEI - National Eye Institute
NIGMS - National Institute of General Medical Sciences
NICHD - National Institute of Child Health and Human Development
NINDS - National Institute of Neurological Diseases and Stroke
FIC - Fogarty International Center
BHME - Bureau of Health Manpower Education
NLM - National Library of Medicine
DRR - Division of Research Resources

Figure 5 (continued)

INTERAGENCY TECHNICAL COMMITTEE: OTHER FEDERAL AGENCIES WITH RELATED PROGRAMS

-USDA-
The USDA funds and administers research concerned with nutrient composition of diet and effect of diet on pathogenesis of atherosclerosis, with blood diseases, and with the etiology of lung diseases linked with agricultural products.

-AEC-
The AEC conducts relevant research dealing with the application of radiation and radioactive isotopes to the understanding of biological processes and to the treatment of heart and vascular disease. Work is also conducted in the application of advanced technology to problems of prosthetics, blood banking and transplantation.

-DOD-
The DOD, via the research activities of the individual services (Army, Navy, Air Force) conducts relevant research, in anticipation of the potential incidence of heart and lung disease in service personnel, and the management of combat injuries involving these organs. Studies in blood banking and transplantation are also conducted.

-EPA-
EPA conducts studies of environmental factors as related to the incidence of heart, blood and lung disease. Programs are directed at the effects of pesticides in the environment and the surveillance of communities to study the correlation of community health with varying levels and types of pollution.

-FDA-
FDA conducts relevant work in the area of blood resources. Primary efforts are directed toward developing standards for laboratory processing of blood, with other efforts in blood fractionation and utilization. FDA's other relevant activity deals with the safety and efficacy of new drugs.

-HSMHA-
Through its major operating components (e.g., RMPS, MCHS, NICHS, etc.), HSMHA funds and administers programs and activities related to prevention, detection and provision of health care services in the area of cardiovascular and pulmonary disease.

-NASA-
NASA supports related mission oriented research directed at understanding, measuring and controlling body functions and mechanisms in diverse environmental states. Instrumentation and techniques have been and are being developed directly applicable to the cardiovascular and pulmonary systems.

-NSF-
NSF supports research in biological processes fundamental to the understanding of cardiovascular and pulmonary disease. Also supported are special programs in biomedical engineering and technological applications.

-SRS-
Relevant research supported by SRS is concerned with rehabilitation of patients who have suffered from cardiovascular and pulmonary disorders. Research is supported directly and through the payment of third party funds.

-SSA-
The SSA supports no research in NHLI related areas; however, the SSA provides third party payments for the provision of care (which may involve participation in clinical research).

-DOT-
DOT funds and administers, through NHTSA, research and development in Emergency Medical Services. The DOT also conducts, through its FAA, research focused on detection and prevention of incipient coronary heart disease.

-VA-
The VA conducts research in most of National Plan problem areas. Projects are supported as part of intramural research and patient care activities in VA hospitals and clinics.

LEGEND:

USDA	-	United States Department of Agriculture
AEC	-	Atomic Energy Commission
DOD	-	Department of Defense
EPA	-	Environmental Protection Agency
FDA	-	Food and Drug Administration
HSMHA	-	Health Services and Mental Health Administration
NASA	-	National Aeronautics and Space Administration
NSF	-	National Science Foundation
SRS	-	Social and Rehabilitation Service
SSA	-	Social Security Administration
DOT	-	Department of Transportation
VA	-	Veterans Administration

Table 2

PROGRAM EXPENDITURES: NATIONAL HEART AND LUNG INSTITUTE, FY 1972

	PROBLEM AREA	GRANTS		CONTRACTS		TOTAL DOLLARS
		NUMBER	FUNDS	NUMBER	FUNDS	
HEART AND BLOOD VESSEL DISEASES	Atherosclerosis	159*	$ 17,239,000	37	$ 9,741,000	$ 26,980,000
	Coronary Heart Disease	126*	18,851,000	25	11,570,000	30,421,000
	Peripheral Vascular Disease	31*	3,137,000			3,137,000
	Hypertension	214*	16,506,000	9	3,971,000	20,477,000
	Stroke	13*	1,664,000			1,664,000
	Congenital & Rheumatic Heart Disease	43*	6,390,000	*	1,000,000	7,390,000
	Cardiomyopathy & Infections of the Heart	4*	2,644,000	*	1,000,000	3,644,000
	Arrhythmias	66*	8,485,000	7	380,000	8,865,000
	Cardiac Failure & Shock	118*	11,836,000	15*	3,072,000	14,908,000
	Multicategorical**	305		35		
	(SUBTOTAL — Heart and Blood Vessel Diseases)	1,081	$ 86,752,000	128	$30,734,000	$117,486,000
LUNG DISEASES	Normal Lung	22***	$ 1,103,000			$ 1,103,000
	Environmental Respiratory Diseases	19	947,000			947,000
	Emphysema/Chronic Bronchitis	91	4,810,000	24	$ 1,775,000	6,585,000
	Pediatric Respiratory Diseases	3	140,000			140,000
	Asthma	7	404,000	1	63,000	467,000
	Interstitial Respiratory Diseases	6	425,000			425,000
	Infectious Respiratory Diseases	7	341,000			341,000
	Sarcoid & Granulomatous Diseases	6	288,000			288,000
	Hypersensitivity Lung Diseases	6	1,029,000			1,029,000
	Pulmonary Vascular Diseases	39	1,349,000			1,349,000
	Hyaline Membrane Disease of the Newborn	21	1,933,000			1,933,000
	Cystic Fibrosis/Other Genetic Lung Diseases	4	101,000			101,000
	Respiratory Failure, Acute	44	1,921,000	21	2,213,000	4,134,000
	Respiratory Failure, Chronic	30	1,437,000			1,437,000
	Extra-pulmonary Effects of Respiratory Diseases	10	637,000			637,000
	(SUBTOTAL — Lung Diseases)	315	$ 16,868,000	46	$ 4,051,000	$ 20,919,000
BLOOD DISEASES	Hemophilia and Other Bleeding Disorders	11	$ 823,994			$ 823,994
	Arterial Thromboembolism	36	2,445,684	1	$ 66,480	2,512,164
	Hemorrhagic Disorders due to Platelet Abnormalities	13	546,689			546,689
	Venous Thrombosis & Pulmonary Embolism	24	993,882	8	410,666****	1,540,571
	Thromboembolism in Relation to Prosthetic Devices	(4)*****	(147,353)			(147,353)
	Microcirculatory Thrombosis	3	418,334			418,334
	Hemoglobinopathies	113	9,492,746	39	4,493,255	13,986,001
	Basic Clotting Studies	53	3,492,746			3,492,746
	Other	24	963,132			963,132
	(SUBTOTAL — Blood Diseases)	277	$ 19,183,431	48	$ 4,970,401	$ 24,153,832
BLOOD RESOURCES	Blood Collection			3	$ 321,340	$ 321,340
	Processing I (Fractionation & Preservation)	9	$ 461,628	13	688,105	1,149,733
	Processing II (Lab Procedures & Controls)	11	1,929,610	23	1,966,273	3,895,883
	Utilization	1	32,700	11	1,561,643	1,594,343
	Distribution & Systems Management			1	37,100	37,100
	Transplantation	30	1,705,964			1,705,964
	(SUBTOTAL — Blood Resources)	51	$ 4,129,902	51	$ 4,574,461	$ 8,704,363
	TOTALS (Grants and Contracts)	1,724	$126,933,333	273******	$44,329,862	$171,263,195
	Other					269,000
	Training					24,905,000
	GRS[a]					8,325,000
	RM&PS[b]					9,552,000
	Intramural					18,259,000
	TOTAL PROGRAM (FY72)					$232,573,000

* Additional Grants or contracts (multicategorical) have been applied to the funds.

** These projects are applicable to more than one category cited and funds have been apportioned accordingly.

*** Excludes $543,000 — Thrombosis.

**** $260,000 of total of $670,666 is counted in Lung Diseases area.

***** $147,353 for 4 grants included in Heart and Blood Vessel Diseases Categories

****** To this total should be added (to obtain institute total number of contracts and reimbursable agreements) 10 from the "Other" category, 46 "no fund" extensions, and 7 "no fund" "other action" extensions — to total 336).

a - general research support grant "contribution" to NIH Division of Research Resources

b - research management and program services.

Table 3

RELATED PROGRAM EXPENDITURES: NATIONAL INSTITUTES OF HEALTH (EXCLUSIVE OF THE NHLI)

	PROBLEM AREA	EXPENDITURES BY NIH COMPONENTS ($000)												PROBLEM AREA TOTAL
		NIAID	NIAMDO	NCI	NIDR	NIEHS	NEI	NIGMS	NICHD	NINOS	FIC	BHME	NLM	DRR	
HEART AND BLOOD VESSEL DISEASES	Atherosclerosis		$1,586		$ 296	$ 259	$ 26	$ 66**	$ 216					$ 779	$ 3,228
	Coronary Heart				163	38		442				$ 95		568	1,306
	Peripheral Vascular				R			73				R		121	194
	Hypertension		550			40R	16R	51	52	$ 268		R		1,964	2,941
	Stroke						23R	97	146	5,306		96R		127	5,795
	Congenital Heart	$ 44			17	164		324	432	*		R		478	1,459
	Rheumatic Heart	239										R		328	567
	Cardiomyopathy		94					324						89	507
	Arrhythmia							179	50	105R		R		421	755
	Cardiac Failure				R			*				17R		222	239
	Shock						50R	382*	52			R		34	518
	SUBTOTAL	283	2,230		476	501	115	1,938	948	5,679		208		5,131	17,509
LUNG DISEASES	Normal Lung	30	25	$ 26	1,097	410		*	337*					249	2,174
	Environmental Respiratory	44		R		965						R	*	32	1,041
	Emphysema and Bronchitis	175				R		10				548		168	899
	Pediatric Respiratory								51			R		48	99
	Asthma	675				44			53			R		146	918
	Interstitial Respiratory											R			
	Infectious Respiratory	863	120			93						R		46	1,122
	Sarcoid and Granulomatous	30		R										15	45
	Hypersensitivity	745										R		20	765
	Pulmonary Vascular							4,300	30	**				135	4,465
	Hyaline Membrane		23					15R	432R					172	642
	Cystic Fibrosis	30	227									R		27	284
	Respiratory Failure							92				R		63	155
	Extra-pulmonary Manifestations			63										11	74
	SUBTOTAL	2,592	395	89	1,097	1,512		4,417	903			546		1,132	12,683
BLOOD DISEASES	Hemophilia	41	15					37				R	*	30	123
	Arterial Thromboembolism		41	R				*				R		60	101
	Hemostasis Disorders	10	90	31				97	27	*		20		252	527
	Venous Thrombosis		R	R				R				R		13	13
	Prosthetic Devices		604					R						40	644
	Microcirculatory Thrombosis			R	23		35	R					*	30	88
	Hemoglobinopathies		3,469	140		14	R	570**	82			R		1,095	5,370
	SUBTOTAL	51	4,219	171	23	14	35	704	109			20		1,520	6,866
BLOOD RESOURCES	Blood Collection			22								R			22
	Fractionation		62	555										239	856
	Laboratory Procedures	169		247						*				41	457
	Utilization		28					238						61	327
	Systems Management														
	Transplantation	6,700	2,155	684*	207		347	677						516	11,286
	SUBTOTAL	6,869	2,245	1,508	207		347	915						857	12,948
	AGENCY TOTAL	$9,795	$9,089	$1,768	$1,803	$2,027	$497	$7,974	$1,960	$5,679		$774		$8,640	$50,006

* = PROJECTS WERE SUPPORTED FOR WHICH FUNDING INFORMATION WAS NOT AVAILABLE
** = PROGRAM PROJECT TOTAL FUNDING WAS AVAILABLE; HOWEVER, ESTIMATES OF AMOUNT OF FUNDING RELATED SPECIFICALLY TO THE NATIONAL PROGRAM WERE NOT AVAILABLE. THEREFORE, TO AVOID OVERSTATEMENT OF RELATED PROGRAMS, FUNOS ARE NOT REPORTED IN THIS TABLE. SEE SECTIONS 1.1.G., 2.10.I, AND 3.7.G OF THIS REPORT
R = RELATED PROJECTS OF NIH COMPONENT ARE DISCUSSED IN A SECTION CROSS-REFERENCED IN THE TEXT OF VOLUME V

LEGEND:

NIAID - National Institute of Allergy and Infectious Diseases
NIAMDD - National Institute of Arthritis, Metabolism and Digestive Diseases
NCI - National Cancer Institute
NIDR - National Institute of Dental Research
NIEHS - National Institute of Environmental Health Sciences
NEI - National Eye Institute
NIGMS - National Institute of General Medical Sciences
NICHD - National Institute of Child Health and Human Development
NINDS - National Institute of Neurological Diseases and Stroke
FIC - Fogarty International Center
BHME - Bureau of Health Manpower Education
NLM - National Library of Medicine
DRR - Division of Research Resources

Table 4

RELATED PROGRAM EXPENDITURES: OTHER FEDERAL AGENCIES

PROBLEM AREA		EXPENDITURES BY FEDERAL AGENCY ($000)												
		USDA	AEC	DOD	EPA	FDA	HSMHA	NASA	NSF	SRS	SSA	DOT	VA	TOTAL
HEART AND BLOOD VESSEL DISEASES	Atherosclerosis	$1,040	$ 500				$ 180		$ 104				**	$ 1,824
	Coronary Heart		4,443	$ 611	$3,121		13,668	$ 840	(R)45	$2,332		$724	**	25,784
	Peripheral Vascular		*460	*				(R)28	R				(R)**	488
	Hypertension	*	(R)540				1,128	171	94				**	1,933
	Stroke		R				3,349	R	23	125			R	3,497
	Congenital Heart				R		1,013	R	R	R			(R)**	1,013
	Rheumatic Heart		R		R		698	R	20	R			R	718
	Cardiomyopathy		(R)111		R		96	R	R				(R)**	207
	Arrhythmia		1,000	*65			16,452	R	R				(R)**	17,517
	Cardiac Failure		(R)				(R)	(R)18	R				(R)**	18
	Shock			476									**	476
	SUBTOTAL	1,040	7,054	1,152	3,121		36,584	1,057	286	2,457		724		53,475
LUNG DISEASES	Normal Lung		695	223	1,134			420	(R)212				(R)**	2,684
	Environmental Respiratory	*	4,448		5,390		3,285	R					R	13,123
	Emphysema and Bronchitis	*	R		R		1,627	R					(R)**	1,627
	Pediatric Respiratory		R				1,850							1,850
	Asthma				R		(R)94							94
	Interstitial Respiratory													
	Infectious Respiratory	*	150	713	R		43						**	906
	Sarcoid and Granulomatous	*												
	Hypersensitivity						R							
	Pulmonary Vascular	*	R	155									R	155
	Hyaline Membrane		30	12			R							42
	Cystic Fibrosis						R							
	Respiratory Failure		R				R	R					R	
	Extra-pulmonary Manifestations		R					48						48
	SUBTOTAL		5,323	1,103	6,524		6,899	468	212					20,529
BLOOD DISEASES	Hemophilia	*	R	12					R					12
	Arterial Thromboembolism		296						R					296
	Hemostasis Disorders	*	R										**	
	Venous Thrombosis		R				55		R				**	55
	Prosthetic Devices		R											
	Microcirculatory Thrombosis		R						R					
	Hemoglobinopathies		1,064	77	147		(1,900)[1]	40	503				**	1,831
	SUBTOTAL		1,360	89	147		55	40	503					2,194
BLOOD RESOURCES	Blood Collection		(R)*					15						15
	Fractionation		(R)537	1,030		$ 50	53	R					**	1,670
	Laboratory Procedures		250	49		425		R						724
	Utilization			370		24	50						**	444
	Systems Management			119			13							132
	Transplantation		1,354	200			523						**	2,077
	SUBTOTAL		2,141	1,768		499	639	15						5,062
TOTAL		$1,040	$15,878	$4,112	$9,792	$499	$44,177	$1,580	$1,001	$2,457		$724		$81,260

* = Projects were supported for which funding data is not available
** = Projects supported as part of intramural research and patient care activities in VA hospitals and clinics - funding data not available
R = Related projects of agency are discussed in a cross-referenced section
(1900)[1] = These are NHLI funds which were expended by HSMHA under a reimbursement agreement. They are included in NHLI program totals (Part I, Volume V)

LEGEND:

USDA - United States Department of Agriculture
AEC - Atomic Energy Commission
DOD - Department of Defense
EPA - Environmental Protection Agency
FDA - Food and Drug Administration
HSMHA - Health Services and Mental Health Administration
NASA - National Aeronautics and Space Administration
NSF - National Science Foundation
SRS - Social and Rehabilitation Service
SSA - Social Security Administration
DOT - Department of Transportation
VA - Veterans Administration

Table 5

RELATED PROGRAM EXPENDITURES: VOLUNTARY ORGANIZATIONS

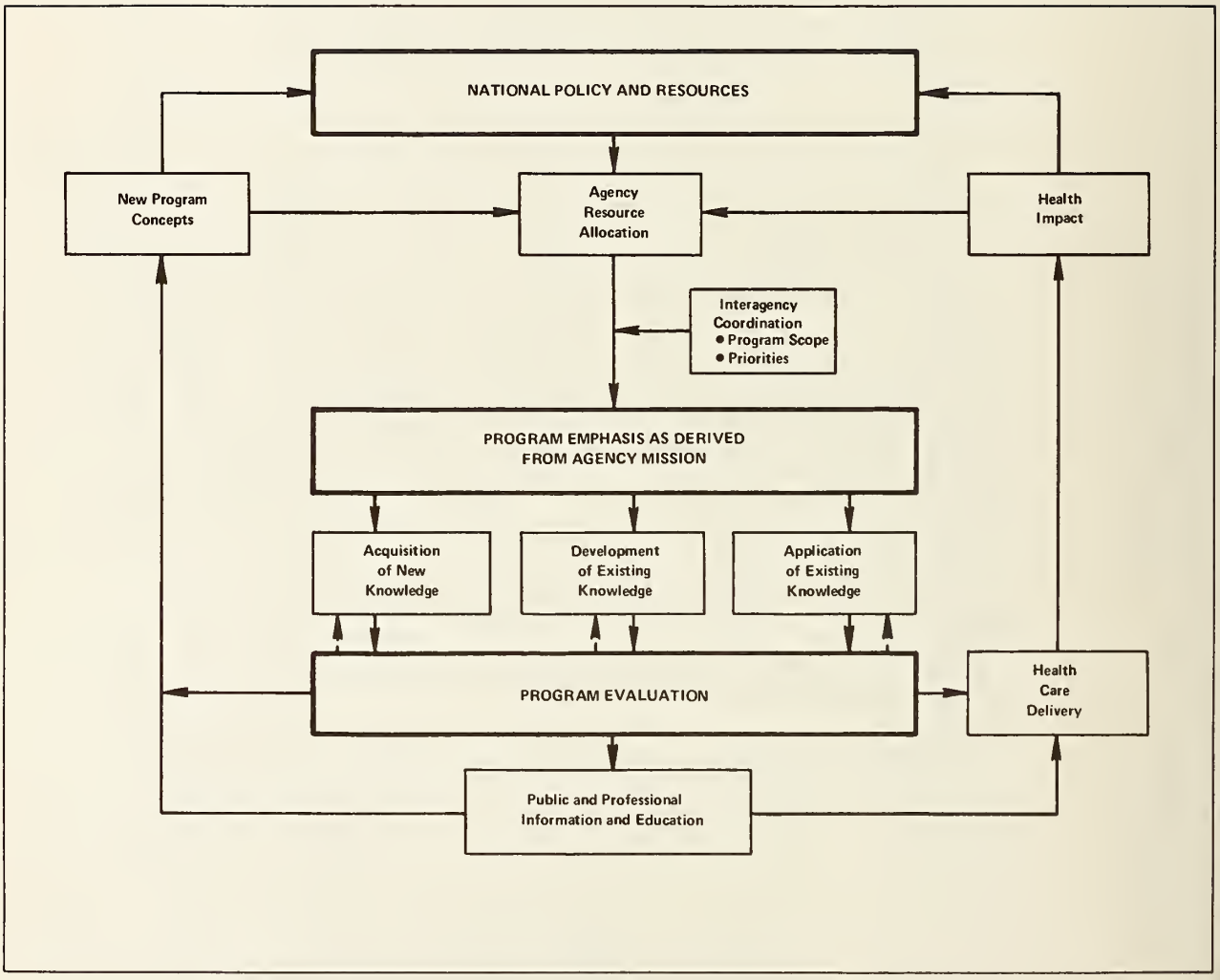
SUPPORTING AGENCY	HEART AND BLOOD VESSEL DISEASES		LUNG DISEASES		BLOOD DISEASES		BLODD RESDURCES		AGENCY TOTALS	
	NUMBER*	DOLLARS	NUMBER*	DOLLARS	NUMBER*	DOLLARS	NUMBER*	DOLLARS	NUMBER*	DOLLARS
AMERICAN CANCER SOCIETY			7(1)	$ 296,841	3	$ 93,493	3	$ 82,411	13(1)	$ 472,745
AMERICAN HEART ASSOCIATION (NATIONAL)	170(2)	$2,286,065	7	101,580	26	361,690	6	90,300	209(2)	2,839,635
(LOCAL)	708(106)	4,914,363	63(11)	372,308	54	357,354	10(1)	69,981	835(118)	5,714,006
AMERICAN MEDICAL ASSOCIATION – EDUCATION AND RESEARCH	11(1)	266,719	9(1)	223,780	3	83,243			23(2)	573,742
AMERICAN PHILOSOPHICAL SOCIETY			1	7,000	1	7,000			2	14,000
BANK OF AMERICA GIANNINI FOUNDATION					1	27,743			1	27,743
CHARLES H. HOOD DIARY FOUNDATION			1	6,500	1	10,000			2	16,500
COUNCIL FOR TOBACCO RESEARCH	11(1)	243,598	21(1)	659,420					32(2)	913,018
DAMON RUNYON CANCER FUND RESEARCH			3	46,950			3(1)	15,500	6(1)	62,450
EASTER SEAL RESEARCH FOUNDATION			1	6,941					1	6,941
FIGHT FOR SIGHT, INC.	1	3,800							1	3,800
FOUNDATION FOR CHILD DEVELOPMENT	1	3,000							1	3,000
HELEN HAY WHITNEY FOUNDATION	1(1)								1(1)	
HERMAN GOLDMAN FOUNDATION			1	12,500					1	12,500
INTERNATIONAL SUGAR RESEARCH FOUNDATION	1	2,688							1	2,688
JOHN A. HARTFORD FOUNDATION	26(3)	1,354,423	14(3)	595,728	11(1)	428,180	2	248,675	53(7)	2,627,006
MINNESOTA FOUNDATION	1(1)								1(1)	
NATIONAL HEMOPHILA FOUNDATION					1(1)				1(1)	
NATIONAL MULTIPLE SCLEROSIS SOCIETY	1	16,071					1	15,104	2	31,175
NATIONAL TUBERCULOSIS & RESPIRATORY DISEASE ASSOCIATION			16	185,136	2	26,346			18	211,482
POPULATION COUNCIL	1	20,000							1	20,000
RESEARCH CORPORATION	2	11,150	1	7,500					3	18,650
ROBERT A. WELCH FOUNDATION	1	50,000					1	12,000	2	62,000
SMITH KLINE & FRENCH FOUNDATION	1	49,100							1	49,100
UNITED CEREBRAL PALSY RESEARCH EDUCATION FOUNDATION	2(1)	25,225	3(2)	29,817					5(3)	55,042
TOTAL	939(116)	$9,246,202	148(19)	$2,552,001	103(2)	$1,395,049	26(2)	$ 533,971	1,216(139)	$13,727,223

*FIGURE IN PARENTHESES INDICATES NO DOLLAR INFORMATION PROVIDED FOR THAT NUMBER OF PROJECTS

THIS TABLE REPRESENTS ALL RESEARCH PRDJECT DESCRIPTIONS REGISTERED WITH THE SMITHSONIAN SCIENCE INFORMATION EXCHANGE FOR THE FISCAL YEAR 1972 PERIOD, AND PROCESSED AS OF APRIL 13, 1973

Figure 6

COORDINATION AND IMPLEMENTATION OF THE NATIONAL PROGRAM



PROGRAM REVIEW AND EVALUATION

The National Heart, Blood Vessel, Lung and Blood Program will undergo annual review, evaluation, and updating by the NHLI, the National Heart and Lung Advisory Council, the Interagency Technical Committee on Heart, Blood Vessel, Lung and Blood Diseases and Blood Resources. Progress reports will be submitted each year to the President and the Congress.

IV. THE NHLI PROGRAM PLAN

The National Heart and Lung Institute Program Plan for an accelerated attack on heart, blood vessel, lung and blood diseases and blood resource problems is presented in this section. In the foregoing discussion, we have defined the major problem areas and outlined the planning process, strategy, coordination and review of the Program. To further the goals of the National Program, the NHLI will promote coordination of projects and initiate new projects directly related to the major problem areas identified by the Institute and its advisors. The goals, opportunities and needs that the NHLI plans to pursue in each of these areas are discussed below. The decisions for action have been influenced by the advice and commentary of the four advisory Panels, the Panel Chairmen, the National Heart and Lung Advisory Council, the Interagency Technical Committee and representatives of other federal and nonfederal organizations. Also considered were current program efforts and the best means for expanding past research efforts. Three major action categories were identified as follows:

- Actions where the current state of knowledge is incomplete and new and basic information must be acquired before methods of prevention, detection, and treatment can be developed
- Actions that draw upon existing information, but require further development and evaluation before application
- Actions that are ready for immediate application in prevention and treatment of disease.

As noted by the Panel Chairmen, the three categories are linked inextricably, one to the other.

The National Heart and Lung Institute Program Plan focuses primarily on two types of program efforts:

- Research Programs
- Prevention, Control and Education Programs.

The Research Programs deal largely with the development of new knowledge and the further evaluation of existing information. The Prevention, Control and Education Programs deal with the application and dissemination of knowledge which has already been developed through research but not yet effectively applied for the prevention and treatment of disease.

RESEARCH PROGRAMS

In this section, research programs are discussed separately for Heart and Blood Vessel Diseases, Lung Diseases, and Blood Diseases and Blood Resources. Under each of these disease problems are discussed major problem areas of disease and/or disorder as presented in Section II, The Problems. For Heart and Blood Vessel Diseases, nine problem areas are discussed; for Lung Diseases, five are discussed; and for Blood Diseases and Blood Resources, three are discussed. Program goals, opportunities and needs, actions and schedules are presented for each problem area.

HEART AND BLOOD VESSEL DISEASES

The Legislative Act charges the Institute to conduct research programs to investigate the epidemiology and etiology of heart and blood vessel diseases, and to study basic biological mechanisms and processes in normal and abnormal phenomena. In addressing this charge, Task Groups and Panels, members of the National Heart and Lung Advisory Council, as well as other advisors and consultants, have identified an

impressive array of opportunities and needs that can be pursued in the heart and blood vessel disease (cardiovascular disease) area at this time. From this advice, the Institute has selected those approaches that appear most promising, most efficient, and are most needed for a National Program.

In the years ahead, it will be vitally necessary and desirable for us to use the nation's manpower and resources in the deliberate pursuit of a variety of research approaches. This section describes such a deployment of our resources in the cardiovascular area.

ARTERIOSCLEROSIS

Program Goals. A large amount of knowledge has been developed about the etiology and pathogenesis of arteriosclerosis. Significant positive statistical associations have been demonstrated between arteriosclerotic disease and hypercholesterolemia, hypertension, physical inactivity, heavy consumption of cigarettes, personality type and other variables. We do not yet know how these variables are associated with arteriosclerosis. However, current research on molecular and tissue interactions has elicited information that promises to explain its development and offer opportunities for prevention.

Clearly, it would be better and less costly to prevent the formation of arteriosclerotic plaques than to attempt to treat the resultant vascular disease and its sequelae. We have many leads to prevention and to a better understanding of arteriosclerosis. Some of these leads come from research on metabolism, normal and abnormal structure and function of the arteries, and genetic and environmental factors which influence atherogenesis. We concur with the priority recommendations of the Heart and Blood Vessel Diseases Panel to "define more completely the pathogenesis of atherosclerosis" and "to conduct controlled clinical trials." We plan to continue research emphasis on pathogenetic mechanisms of arteriosclerosis and to evaluate preventive measures in clinical trials.

- Our overall goal in arteriosclerosis is to obtain better understanding of its basic process and to improve the prevention, diagnosis and treatment of the process and its sequelae.

Opportunities and Needs. All aspects of the study of arteriosclerosis would be greatly advanced if we had diagnostic instruments for detecting small changes in atherosclerotic plaques. The present state of technological development suggests that this is possible. Current approaches include highly sophisticated techniques such as ultrasonic methods, x-ray densitometry and computer-assisted image enhancement of complex image signals. These techniques are not yet adequate, but indicate a feasible and promising technical area where rapid and successful progress can be expected.

Many needed studies of chronic arterial disease cannot be conducted in man. Suitable animal models of human disease would bring about many economies of time and effort in the attack against arteriosclerosis. Nonhuman primate models with chronic experimental arteriosclerosis and chronic experimental hypertension need to be developed. These animals would allow us to study the maintenance and regression of atherosclerotic plaques, local biochemical and cellular changes in advanced plaques, and treatment of advanced plaques. Animals with spontaneous metabolic disease such as hyperbetalipoproteinemia (elevated blood lipids) or diabetes need to be bred to create colonies for research in these disorders related to arteriosclerosis.

Recent studies have shown genetic influence on the metabolism of lipoproteins, on the excretion of sterols and on the atherogenetic reaction of the arterial wall. This research, presently incomplete and in need of both confirmation and detailed investigation, will be fundamental to the identification of patients at high risk of arteriosclerosis and to the development of rational treatment.

We need to emphasize a strong, general research program in the pathogenesis of arteriosclerosis, stressing studies of lipoproteins and their modification by drugs, diet or surgery. Parallel progress that has been made in recent years in cellular research, enzyme studies, collagen and mucopolysaccharide chemistry now allows sophisticated research on the tissue of the artery wall and its role in plaque formation. In addition, current population studies in the Institute's Lipid Research Clinics and Specialized Centers of Research in Arteriosclerosis have identified a need for new and sophisticated investigations to clarify the role of nutrition in the development and treatment of arteriosclerosis.

Chronic diseases like arteriosclerosis take years to become clinically overt. In the interval, the individual may appear to be in good health. The results of research and development must reach the community through programs in health education, public motivation and compliance with preventive or therapeutic

regimens (see section on Prevention, Control and Education Programs).

Several clinical trials are currently underway to seek ways to prevent coronary heart disease. These efforts are aimed at determining the value of controlling the risk factors of high blood lipids, high blood pressure, and smoking. Potentially useful drugs are under study. Such trials of potential preventive measures have both theoretical and practical value. The efficacy of intestinal surgery (ileal bypass) in high risk patients with high blood lipids needs to be further evaluated. Controlled comparison of surgical versus medical management should be done to evaluate these forms of treatment.

Actions. To meet these needs and to take advantage of the opportunities in arteriosclerosis research, the Institute plans to:

1. Emphasize pathogenetic studies within existing research programs, centers of research and lipid research clinics. Special emphasis will be given to nutritional research and studies of the vessel wall and its relationship to arteriosclerosis.

2. Stimulate the development of sensitive, noninvasive, convenient and safe diagnostic techniques that can be used to determine arteriosclerotic changes in vessels.

3. Establish colonies of suitable animal models with particular reference to nonhuman primates with arteriosclerotic disease for use in arteriosclerosis research.

4. Expand current population studies in the Institute's Lipid Research Clinics, Specialized Centers of Research in Arteriosclerosis, and Clinical Applications and Prevention Programs, to include in-depth genetic studies. Animal research will be encouraged in genetics related to arteriosclerosis.

5. Encourage experts in psychosociology and behavioral research to study the problems associated with health education and attitudes, motivation and compliance as these relate to the prevention, therapy and rehabilitation of patients with arteriosclerosis, hypertension or stroke (see section on Prevention, Control and Education Programs).

6. Expand collaborative clinical trials, particularly with reference to the control of abnormal lipid metabolism and prevention of coronary heart disease.

Schedule. Present programs relating to the prevalence of lipid abnormalities and of hypertension among children will be completed between FY 76 and FY 78. Program action will be continued or initiated in pathogenesis, instrumentation, animal models, behavioral studies, and clinical trials. These are projected to increase by about 20 percent over the next five years.

HYPERTENSION

Program Goals. High blood pressure can be controlled and we know that such control results in a reduced incidence of stroke and heart failure, and perhaps also reduced incidence of heart attacks.

The etiology and pathogenesis of the most common form of hypertension is not understood and continuing research will be necessary to elucidate this. Because of the large numbers of people affected by hypertension, it would be especially desirable to be able to prevent it. Indeed, the National Heart and Lung Advisory Council has stated, "The Council gives high priority to investigation of the causes of hypertension."

- The long-range goal in hypertension is to prevent it; the short-range goal is to optimize the utilization of effective treatment which currently exists.

Opportunities and Needs. We do not know how beneficial treatment of mild forms of high blood pressure is. Since an estimated 19 million people have mild hypertension, it is important that this information be developed. The Panel Chairmen have given high priority to clinical therapeutic trials on mild-to-moderate hypertension.

About four million people at any given time have hypertension of a degree known to be harmful. It can be controlled by medication with appropriate drugs. However, currently available drugs require close medical supervision and often have unpleasant side effects which make it difficult to use them for long periods of time in asymptomatic individuals. We need to develop improved pharmacologic agents without such side effects and without the need for meticulous, individually adjusted dosage.

Rational treatment and prevention of hypertension will require a thorough understanding of its etiology and

pathogenesis. While some current information about the formation and modulation of vasopressor polypeptides and related enzyme systems helps to explain pathogenetic mechanisms, we know little about etiology. An intensive examination of the etiology and pathogenesis of hypertension is essential.

Actions. To meet these needs and to take advantage of these opportunities, the Institute will:

1. **Emphasize research on the etiology and pathogenesis of hypertension, including its epidemiology, in many of the individual and specialized laboratories working on this difficult problem.**

2. **Implement the hypertension program described in the section on Prevention, Control and Education Programs and the behavioral research program described in Action 5 under Arteriosclerosis.**

3. **Conduct a pilot clinical trial of antihypertensive therapy in mild hypertension in collaboration with the Veterans Administration. The purpose of this trial will be to evaluate the beneficial effect of treatment of mild-to-moderate hypertension on major vascular complications such as stroke and heart attacks. The NHLI and the Veterans Administration have discussed a research plan to study the feasibility of conducting a controlled clinical trial to reduce the incidence of first heart attacks in persons with diastolic blood pressure levels of 90 to 105. We need to find out whether or not these persons should receive treatment which may be required for their lifetime. Future implementation of a definitive trial will depend on accession of sufficient participants from the Veterans Administration facilities or from community populations. As presently planned, the feasibility phase would be initiated in FY 74 and would be expanded in FY 75. The study would extend beyond FY 79.**

4. **Evaluate new pharmacologic approaches to the treatment of hypertension utilizing existing research centers and pharmacologic expertise, with emphasis on new drug formulations and diagnostic and monitoring instrumentation. It is not our intention to engage in development that might better be done by the pharmaceutical industry.**

Schedule. Present programs will continue to receive emphasis. The prevalence studies of hypertension in children will be completed as mentioned in the Arteriosclerosis section.

Continuing and new actions will increase slightly in FY 74 and increase further by about 70 percent by FY 79. An appreciable part of this increase is attributable to the clinical trial of therapy for mild hypertension. Additional increases will occur in the pathogenesis and pharmacology of hypertension.

CEREBROVASCULAR DISEASE

Program Goals. The National Institute for Neurological Diseases and Stroke is primarily responsible for programs on those aspects of stroke that deal with brain injury and its consequences. The NHLI is responsible for programs on the cerebrovascular pathology that underlies the stroke. A liaison Joint Council Sub-committee exists for purposes of coordination and exchange of information.

- The goal of the NHLI program is to decrease the incidence of stroke through studies of the pathology and pathogenesis of cerebrovascular disease.

Opportunities and Needs. As noted in the priority recommendation of the Heart and Blood Vessel Diseases Panel, to determine the etiology and prevention of hypertension, we need to conduct animal studies of the effects of chronic arteriosclerosis and chronic hypertension on the arteries of the brain. The goals of these animal studies will be to elucidate, by methods not applicable to man, the vascular pathology that leads to stroke.

The opportunities and needs discussed in the sections on Arteriosclerosis and and Hypertension also apply to Cerebrovascular Disease.

Actions. To deal with the cardiovascular problems which form the basis for cerebrovascular disease and stroke, the Institute will:

1. **Conduct animal studies on the vascular lesions associated with cerebrovascular disease and stroke. The chronic and special animal resources referred to in the sections on Arteriosclerosis and**

Hypertension can be utilized with minor expansion and redirection for the study of cerebrovascular disease at modest additional cost.

2. Implement the related studies discussed in the sections on Arteriosclerosis and Hypertension.

Schedule. New actions in animal studies will increase the current effort in this area by about 70 percent between FY 74 and FY 79.

CORONARY HEART DISEASE

Program Goals. A research program focused on patients with acute heart attacks has developed information about pathophysiology; prognostic factors; pharmacological, surgical, and circulatory assist therapy; and techniques and instruments for conducting research in the acutely ill patient. These developments can now be built upon and more broadly used.

- A primary goal of the program is to develop improved therapy, rehabilitation, diagnosis, and improved understanding of the mechanisms resulting in symptomatic coronary disease.

Coronary artery bypass surgery has been developed in recent years, primarily for treating angina pectoris. This technique uses a blood vessel graft to bypass a narrowed or occluded segment of a coronary artery. Over 20,000 such operations are now done annually with hospitalization costs in excess of $5,000 for each operation.

- A major goal is to establish the indications for and the effects of coronary artery surgery in the treatment of various forms of coronary heart disease.

Each year, 400,000 deaths from coronary heart disease occur suddenly or before hospitalization. Half of these occur instantaneously and are unwitnessed. Either heart disease or hypertension is evident in 300,000 of these deaths, but in 100,000, sudden cardiac death is the first evidence of heart disease.

- Another major goal of the program is to develop and assess emergency medical care methods for heart attack victims and to develop and assess prophylactic treatment with drugs to prevent sudden cardiac death.

Prior clinical and fundamental research has provided knowledge of the causes, diagnosis, and treatment of coronary heart disease. This work is the basis upon which targeted research efforts can now be mounted. In addition to topics identified under Coronary Heart Disease, closely related work is included in the sections on Arteriosclerosis, Arrhythmias, Heart Failure and Shock, and in the section on Prevention, Control and Education Programs.

Opportunities and Needs. The emphasis upon patient-oriented research must shift from a focus upon acute heart attack to inclusion of other important aspects of coronary heart disease—angina pectoris, heart failure, and arrhythmias. Particular attention must be paid to further development and evaluation of therapy, rehabilitation, measurement techniques suitable for use in patients, and answers to the fundamental question of why chronic coronary heart disease is finally manifested as heart attack or sudden death. These areas of research have been emphasized by the members of the Heart and Blood Vessel Diseases Panel and the National Heart and Lung Advisory Council. The study of susceptible patients requires specialized facilities that are complex, expensive, and staffed with personnel who are available for emergencies. Importantly, such specialized cardiological facilities will be very useful for research on other forms of heart disease.

It is widely recognized that coronary artery surgery brings relief of symptoms for a majority of patients with angina pectoris. However, its benefits and side effects, its value compared to conventional drug therapy, and its effects upon lifespan and quality of life require further research.

Recent research has shown that the final step in sudden cardiac death is usually ventricular fibrillation, a chaotic disturbance of the heart rhythm. This disturbance can now be treated by intravenous administration of drugs. Thus, the importance of finding drugs to prevent ventricular fibrillation in high risk patients is obvious. We need to find agents that can be taken for long-term prophylaxis as well as drugs that can be used immediately upon the development of symptoms of heart attack.

The high frequency of out-of-hospital deaths and the favorable experience with improved systems of emergency cardiac care underscore the need for further development of emergency-related techniques and resources for use in cardiac patients.

Development and testing of new hypotheses and methods are critical to continued clinical and fundamental research into the cause, diagnosis, and treatment of coronary heart disease.

Actions. To meet these needs and to explore the identified opportunities, the Institute will:

1. **Establish Specialized Centers of Research in Coronary Heart Disease in two stages at approximately 12 locations. These will emphasize the various manifestations of coronary heart disease, but will also be used for other forms of heart disease. The centers program will include comprehensive clinical investigations supported by closely related, fundamental laboratory studies.**

2. **Complete the final planning for a collaborative national program to establish indications for and the effects of coronary artery surgery. This plan involves randomized studies to compare surgical and medical management in carefully defined groups of patients with coronary heart disease but with different symptoms. About 6,000 patients will be involved. We also plan to develop a registry to follow 15,000 patients in whom the indications for surgical or medical treatment seem sufficiently clear that randomized allocation might be improper—but in whom follow-up clinical data is of critical national importance.**

3. **Develop and test early care methods and instrumentation for cardiac patients at risk of sudden death. These methods must be suitable for incorporation into emergency medical care systems. Concurrent efforts will be directed toward the design, pilot testing, and subsequent large-scale clinical trials of antiarrhythmic drugs for long-term prevention in high risk patients and for immediate administration upon development of heart attack symptoms.**

Schedule. The present long-term study of lipid-lowering drugs aimed at preventing recurrence of heart attack or death from coronary heart disease (the "Coronary Drug Study") will be essentially completed in FY 74 and terminated by FY 75.

The Myocardial Infarction Research Units, which have focused upon heart attacks, will be discontinued in FY 75. Less emphasis will be placed on collecting extensive hemodynamic data and other descriptive data in patients with varying severity of heart attack.

Continuing and new actions in coronary heart disease will emphasize manifestations other than heart attack, particularly angina pectoris and sudden cardiac death. These actions will be accomplished, in part, by the development of Specialized Centers of Research in Coronary Heart Disease. The emphasis will shift toward electrophysiological and surgical investigations, with specific attention to prevention of acute events. Multidisciplinary and other approaches will be followed.

PERIPHERAL VASCULAR DISEASES

Program Goals. Peripheral vascular diseases are the cause of considerable suffering and disability. Surgeons have developed techniques to replace diseased peripheral artery segments with vascular or prosthetic grafts. Otherwise, peripheral arterial disease has been the focus of only a limited research effort, and peripheral venous disease has received even less emphasis.

- The goals of the program are to improve diagnosis, therapy, and rehabilitation, and to improve understanding of the mechanisms causing peripheral arterial and venous diseases.

Opportunities and Needs. We must develop methods for diagnosing vascular diseases before they reach an advanced state, for more effective medical management, and for extending surgical therapy to small vessels. Understanding the basic cause of the diseases is most important and will require study of the role of neural control of vascular tone, mechanism of action of smooth muscle, pathogenesis of peripheral atherosclerosis, and the importance and significance of risk factors.

Actions. To meet the needs and to take advantage of the opportunities to improve the management of peripheral vascular diseases, the Institute will:

1. Implement the programs described in the section on Arteriosclerosis, and the programs on non-invasive instrumentation, discussed in the section on Bleeding and Clotting Disorders. This is in accordance with the Panel Chairmen's priority recommendation to encourage the development of engineering techniques for early detection of peripheral vascular diseases.

2. Encourage clinical and basic scientists to study the causes, diagnosis, and treatment of diseases of the peripheral arteries and veins.

Schedule. Continuing and new actions on peripheral vascular diseases will emphasize clinical and basic investigation. Emphasis will be on diagnostic techniques for small vessels, and the relation of physiology and pathophysiology to clinical manifestations of disease. Multidisciplinary approaches will be emphasized as well as specific approaches.

ARRHYTHMIAS

Program Goals. Important new concepts are developing concerning the arrhythmias that occur immediately upon coronary occlusion and those which occur at a later time. These may be different types of altered electrical activity and may require different types of drug therapy. Current drugs aimed at controlling arrhythmias may have side effects causing alterations of the workload of the heart and possibly myocardial damage.

- A major goal of the program is to develop methods for the prevention of arrhythmias which cause sudden cardiac death.

Identification of arrhythmias that carry a high risk of sudden cardiac death is fundamental to preventive measures and was emphasized by the Heart and Blood Vessel Diseases Panel as well as the National Heart and Lung Advisory Council. The analysis of spontaneous rhythms and the influences of drugs must be assessed by quantitative analysis of extensive electrocardiographic tape recordings. Substantial progress has been made toward performing this task automatically, rapidly, and quantitatively by computers.

Arrhythmias and other electrical disturbances of the heart cause important symptoms and aggravate many forms of heart disease.

- Another important goal of the program is to improve currently available methods for prevention, diagnosis and management of arrhythmias and other electrical disturbances of the heart.

Opportunities and Needs. Improved understanding of the electrical behavior of ischemic heart muscle is essential to the prevention of sudden cardiac death. Several drugs which are effective agents in the setting of the coronary care unit need to be evaluated for benefits and side effects as prophylactic agents in patients suspected of having myocardial infarction. Particular attention needs to be paid to the effect of heart rate upon automaticity and rhythm disturbances and upon the workload and consequent potential damage to the heart. Drugs which have antiarrhythmic actions, which can be taken orally over long periods of time, and which have shown promise in limited clinical trials, need to be evaluated in larger scale trials. Fundamental to all these clinical studies is the development of systems for quantifying electrocardiographic signals automatically and rapidly.

In addition to the efforts focused upon ventricular fibrillation and the prevention of sudden cardiac death, disturbances of the conduction system of the heart, as well as other important rhythm disturbances, must be managed more effectively.

Actions. To meet these needs and to explore emerging opportunities for the control of arrhythmias, the Institute will:

1. Expand current programs for the prevention of arrhythmias causing sudden cardiac death. These programs will focus on the development of

automated, quantitative analysis of electrocardiographic signals, and clinical studies to identify chronic or intermittent disturbances of rhythm which indicate a high risk of sudden death. Studies of electrophysiology and therapy of rhythm disturbances associated with inadequate blood supply to the heart muscle will also receive emphasis.

Schedule. It is anticipated that the current emphasis on descriptive aspects of conduction disturbances will be concluded. Continuing and new actions related to arrhythmias will emphasize those fundamental to understanding sudden cardiac death. There will be an overall expansion of program activity with a peak in currently projected programs in FY 76 and FY 77, and subsequent levelling off activity by FY 79.

HEART FAILURE AND SHOCK

Program Goals. The National Heart and Lung Advisory Council, the Panel Chairmen and the Heart and Blood Vessel Diseases Panel all give priority to studies of heart failure. In a heart attack, blood supply to a part of the heart muscle becomes so severely reduced that the muscle undergoes irreversible damage. It can no longer contract or pump, and is ultimately replaced by scar. The amount of irreversibly damaged muscle is not predetermined at the onset of the attack; there is a zone which is in jeopardy but has not yet progressed to the point of no return. Current research has identified several promising means for protecting this zone of potentially reversible damage and for promoting its recovery. Some of thse approaches are now at the stage of initial clinical feasibility trials; others have shown promise in animal studies.

- A major goal of the progam is to minimize heart failure associated with and following heart attack by enhancing the survival of damaged heart muscle.

Methods to quantify the amount of heart muscle which is inadequately perfused or which has undergone irreversible damage are crucial to the evaluation of therapeutic interventions. Recently, several such methods have shown promise. They may make it possible to test new approaches more economically and in fewer patients than is now required for evaluation by clinical criteria.

Research and development of devices and techniques for patients with these diseases have been supportive of more conventional forms of drug and surgical treatment. It has become increasingly apparent that the availability of heart devices and diagnostic instrumentation for monitoring and supporting the circulation would permit identification of a larger number of patients needing treatment and monitoring. These developments would offer significant additional modes of therapy for patients with heart failure and shock, as well as other heart and blood vessel problems.

- A goal of the program is to develop and apply a variety of therapeutically effective, safe and reliable cardiac assist and total replacement heart devices and supporting diagnostic and monitoring instrumentation.

Opportunities and Needs. Current therapy to enhance the survival of ischemic heart muscle must be evaluated in larger scale by more definitive clinical studies than those now underway. The effects upon infarct size must be quantified and survival assessed. Ischemic heart muscle must be studied at the cellular and subcellular levels, in an effort to develop more effective therapy.

We need to validate the techniques for quantifying the degree of heart muscle damage. Subsequent use of those found valid would minimize the number of patients needed for evaluation of new modes of therapy. Electrocardiographic, enzymatic and radioisotopic techniques show promise.

Studies of heart failure and shock need to be expanded to include other organ systems. Thus, as the National Heart and Lung Advisory Council has recommended, the dynamics and the neural and endocrine control of the circulation must be studied in the periphery as well as in the heart, kidney, and other organs.

Actions. To meet these needs and to explore the opportunities, the Institute will:

1. **Continue biochemical and physiological studies of the fundamental processes associated with heart muscle survival, both in laboratory and in clinical studies, to minimize the extent of heart**

muscle damaged in a heart attack. Based on current pilot studies, it is expected that studies in patients can be carried out on a sufficiently large scale to gain definitive answers.

2. Expand current programs for quantifying the extent of heart muscle which is inadequately perfused or which has undergone irreversible damage.

3. Expand development efforts in emergency and temporary circulatory support devices directed at short-term treatment of serious cardiovascular insufficiencies, especially heart failure and shock, until the clinical condition can be stabilized and reversed.

4. Intensify development and testing of implantable artificial heart assist devices, including power and control components, capable of taking over a significant portion of the physiological work of the heart for extended periods of time or the remainder of the patient's life in cases where adequate cardiac function cannot be achieved through conventional means, such as surgery or drugs.

5. Expand research and development efforts of partially and totally implantable artificial hearts with increased emphasis on new opportunities in materials, power and control systems, and design and function of the heart, to develop effective treatment modalities for patients in cardiac failure for whom no other treatment exists.

6. Implement research on the physiology of circulatory support, mechanics of blood flow, and blood materials interaction in prosthetic devices.

7. Expand research and development on noninvasive and invasive techniques for detection of arteriosclerotic lesions (see section on Arteriosclerosis), monitoring of cardiac performance, detection and monitoring of pediatric cardiac diseases (see section on Congenital and Rheumatic Heart Diseases), and on long-life cardiac pacemakers and improved heart valves.

Schedule. Continuing and new actions related to cardiac failure and shock will emphasize the pathophysiology of ischemic myocardium and methods of quantifying this condition, as well as directing attention to systemic responses to heart failure and shock. Clinical trials will be ready for phase-in in FY 75; a number of promising techniques have progressed to a stage where they are ready for clinical evaluation on a moderate scale. These new efforts will be initiated in FY 74, peak in FY 75 and phase down by FY 79.

Present programs on invasive methods for measuring blood pressure, blood flow, and other cardiac performance parameters, certain techniques of circulatory assistance and replacement, and selected biomaterials programs will be terminated as targeted objectives are met. This selective termination of activities will reduce current commitments in FY 74. These resources will then be redirected to the new actions which will increase through FY 78 with a subsequent levelling of activity as objectives are met.

CONGENITAL AND RHEUMATIC HEART DISEASES

Program Goals. The earliest surgical successes in the treatment of heart diseases were in the correction or palliation of congenital heart disease. These successes are being expanded in the development of diagnostic and surgical techniques applicable to the newborn. Important insights have also been gained into the development of the cardiovascular system.

- The major goals of the program are to understand better the causes of congenital heart disease, to improve diagnosis and therapy, and to rehabilitate patients with congenital heart disease, particularly the newborn.

Rheumatic heart disease is an immunological disturbance that frequently occurs years after initial rheumatic fever and prior streptococcal infection. Improved understanding and control of immunological problems could thus be important in the identification of susceptibility and the prevention of rheumatic heart disease, as well as in the success of cardiac transplants and in the prevention or treatment of cardiomyopathy and possibly other forms of heart disease.

- Another important goal is to attain a better understanding of the immunological problems associated with heart diseases.

Closely related programs are discussed in the section on Prevention, Control and Education Programs, and deal

with the management of congenital heart disease in the newborn and motivation of patients to adhere to long-term drug therapy needed in the prevention of rheumatic heart disease.

Opportunities and Needs. Essential to the prevention of congenital heart diseases is a better understanding of the causes and the normal development of the cardiovascular system. The National Heart and Lung Advisory Council has recommended that the Institute conduct an "intensive interdisciplinary study of all aspects of the etiology and pathophysiology of congenital heart disease and the neonatal cardiovascular system." The role of maternal infection and toxic exposures are particularly relevant. The emphasis on diagnosis, therapy, and rehabilitation of congenital heart disease patients must increasingly involve the newborn as well as school age children. The Panel Chairmen have recommended that the National Program should "assure the first few hours of life."

The roles and nature of immune mechanisms as they relate to the heart need to be better understood. Therapy for the suppression of harmful immunological responses must be developed and evaluated.

Clinical and fundamental research relevant to causes, diagnosis and therapy of congenital heart disease, rheumatic fever, and rheumatic heart disease must be continued with periodic updating of approaches.

Actions. To meet these needs and to explore the identified opportunities, the Institute will:

1. **Establish Specialized Centers of Research in Congenital Heart Disease at two to four locations in FY 75 and an additional two to four locations in FY 78. These centers will combine research on cardiovascular development in the fetus and newborn with improved diagnosis and therapy, particularly in the newborn, utilizing improved techniques and instrumentation.**

2. **Establish a targeted effort to study immunological problems in heart disease and their management, specifically in relation to rheumatic heart disease, cardiac transplantation, and cardiomyopathies (see Transplantation Biology in section on Blood Resources).**

Schedule. There will be a diminished emphasis on the hemodynamic and surgical aspects of these diseases in older children and adults. The continuing and new actions will emphasize the causes of both congenital and rheumatic heart diseases. In coordination with the National Institute of Child Health and Human Development, the National Heart and Lung Institute will give special attention to the role of infections, drugs and other toxic exposures during pregnancy in congenital heart disease. For congenital heart diseases, there will be an increasing clinical emphasis on the neonatal period.

CARDIOMYOPATHY AND INFECTIONS OF THE HEART

Program Goals. Cardiomyopathies and infections of the heart are increasing in frequency. The importance of toxic substances, viral infections and immunological phenomena is widely recognized, although a number of causes remain unknown. Accordingly, the Heart and Blood Vessel Diseases Panel give priority to identification of the etiologies of cardiomyopathy. The advent of antibiotics has substantially diminished heart disease caused by bacterial infections. However, new problems have arisen, such as infections on prosthetic heart valves.

- The goals of the program are to prevent, diagnose, and treat the various cardiomyopathies and infections of the heart, with particular emphasis on improved understanding of their causes.

Opportunities and Needs. We need to understand the causes of cardiomyopathies and myocarditis. The roles of toxic substances, including drugs and alcohol, and of viral infections and genetic disorders need to be investigated. Cellular and subcellular biochemical and immunologic studies offer opportunities of improved understanding of these problems. We need to develop better diagnostic and therapeutic approaches to these diseases. Since these diseases stem from a variety of causes, research efforts need to be broadly based and involve multiple disciplines.

Action. The Institute will:

1. **Focus attention on studies of the etiologies of cardiomyopathies and infections of the heart, emphasizing epidemiological methods, viral and immunological research, development and utilization of animal models, and the determination of the mechanisms of myocardial damage by applications of biochemical, physiological, physical and pharmacological techniques (see also section on Congenital and Rheumatic Heart Diseases, Action 2).**

Schedule. Continuing and new actions, with emphasis on studies of causation, will increase gradually until FY 78 with subsequent plateauing.

LUNG DISEASES

The Institute's plan for a program against lung diseases draws upon the recommendations of the Lung Diseases Panel and the National Heart and Lung Advisory Council. It is responsive to the Legislative Act which encourages new attention to chronic lung diseases, including the establishment of research and demonstration centers. After reviewing the recommendations and the Legislation in the light of available resources and the current state of relevant knowledge and technology, we have defined a program of feasible dimensions addressed to both immediate and long-range objectives. Specific proposals which are of comparable importance and urgency are to:

- Use available knowledge and technology to solve specific problems whose solution will have an immediate impact on public health

- Address well-defined diseases which constitute national health problems, but whose etiology, natural history, diagnosis and effective treatment have been inadequately investigated

- Conduct studies of the structure and function of the lung in order to gain information which will lead to improvement in prevention and treatment for the whole spectrum of lung diseases.

Program needs and actions addressing these proposals are discussed in this section and directed toward respiratory diseases exclusive of cancer of the lung, upper respiratory infections and pulmonary tuberculosis.

The lung programs of the National Heart and Lung Institute deal with four disease categories: Pediatric Pulmonary Diseases, Emphysema and Chronic Bronchitis, Fibrotic and Immunologic Lung Diseases, and Respiratory Failure. These problems are defined above in Section II, The Problems. Fundamental to the research conducted to alleviate health problems resulting from these diseases are studies of the Structure and Function of the Lung, a fifth program area.

STRUCTURE AND FUNCTION OF THE LUNG

Program Goals. Past pulmonary research has focused on studies of the respiratory physiology of the lung. While this has provided a basis for diagnosis, it has not contributed to our understanding of disease etiology and mechanisms. Advances in such basic disciplines as biochemistry, immunology, and ultrastructural anatomy, offer new opportunities to us, for the major missing element in our understanding of the respiratory disease process is knowledge of the cellular and molecular biology of lung tissue. The Lung Diseases Panel, the Panel Chairmen, and the National Heart and Lung Advisory Council agree that the study of the lung and its biology is of highest priority. A better understanding of lung tissue biology would lead to major advances in combating emphysema, chronic bronchitis, pulmonary fibrosis, immunologic lung diseases, respiratory distress of children and respiratory failure.

- While it is essential to first focus studies on the cellular biology of the normal lung, the ultimate goal of the program is to increase understanding of the disease processes and to develop effective methods for prevention, diagnosis and therapy of lung diseases.

Opportunities and Needs. We believe that an expanded emphasis on studies of the basic structure, function and metabolism of the lung are needed at this time. These studies should include the quantities, composition, and mechanisms of development of the various components in normal lung tissues, their chemical precursors and their possible variations with age, sex and environmental influences. We do not know how variations in structural proteins, lipids, and hormones, are involved in diffuse pulmonary fibrosis and in various types of obstructive disease of the airways. The *in vivo* balance and interaction among proteolytic enzymes need to be determined since they have potential for altering the connective tissue in the lungs.

Improved knowledge about the structure and function of the various cell types making up normal lung tissue is important, as loss and replacement of these cells play a major role in the development of many lung diseases. Measurements of turnover rates of lung cells and alterations in these rates with disease require further study. Ultrastructural investigations will play an essential role

in the development of this information as will efforts to isolate and characterize individual cell types.

We need to know more about the lung's defense mechanisms, since the failure of these may play an important part in disease processes. Bronchial mucus is one of the factors in the defense mechanisms of the lung. The structure synthesis, physical and physicochemical characteristics of this substance need to be elucidated. The cilia in the bronchial tree are another vital defense mechanism, and investigations of the structure and function of cilia are crucial in understanding lung clearance and host defense.

A number of classical areas of pulmonary physiology require continued study and correlation with new knowledge of cellular biology, structure and function. However, we have elected to reduce the present level of effort in these areas. The ongoing physiologic studies focus on the mechanical properties of the lungs and the pulmonary blood vessels, and the coupling of mechanical events to the neurophysiological regulation of ventilation.

Actions. To meet these needs for increased information and to take advantage of the opportunities presented by modern investigative techniques, the Institute will:

1. Encourage investigator-initiated research in metabolism, cellular biology, and defense mechanisms of the lung. This will be supplemented as needed by targeted research addressed to topics not adequately covered by investigator-initiated research.

2. Develop multidisciplinary approaches, such as program projects or Specialized Centers of Research, in the area of normal lung structure and function. In addition, we will initiate new types of targeted programs for collaboration between fundamental and clinical disciplines. These broad-based programs will require the collaboration and exchange of information between basic scientists such as biochemists, immunologists, and cell biologists, who are not yet focusing on the lung, and pulmonary specialists who need to develop information in basic science areas.

Schedule. Present programs relating to structure and function of the lung, not included in the planned priority actions, will be reduced. Studies on the pathophysiology of the lung, especially respiratory mechanics and gas exchange will be concluded. Continuing and new actions in pulmonary structure and function will be divided between multidisciplinary and specific approaches with gradually increasing activity through FY 79.

PEDIATRIC PULMONARY DISEASES

Program Goals. Despite recent advances in our knowledge, the cause of respiratory distress syndrome of the newborn, the nature of cystic fibrosis, and the possible long-term effects of early childhood bronchiolitis remain obscure.

- Until hyaline membrane disease can be prevented, early diagnosis and prompt initiation of therapy are essential to save the lives of babies born with this disorder. Primary goals of this program are to develop improved methods for early diagnosis and to design more effective modes of therapy.

- Because cystic fibrosis is a genetically determined disease for which present modes of therapy are at best palliative, the primary goal at this time is to develop a rational basis for therapy through an understanding of the pathogenesis of this disease.

- There is reason to believe that bronchiolitis in children may be related to chronic lung disease in the adult. Therefore, an important goal is to conduct long-term follow-up, epidemiologic studies of children who have had bronchiolitis.

These program goals are in accordance with the interests of the Lung Diseases Panel, the Panel Chairmen and the National Heart and Lung Advisory Council, in the development of diagnostic methods for hyaline membrane disease study of the pathogenesis of cystic fibrosis, and investigation of the development of bronchiolitis.

Opportunities and Needs. Fundamental studies are needed to elucidate the biochemical changes associated with hyaline membrane disease and to develop methods to detect these changes prenatally so that therapy can be initiated promptly at birth. It is also necessary to determine basic biochemical defects which are caused by the gene for cystic fibrosis, and which lead to alterations in body fluids and tissues. Effective therapy will depend upon an improved understanding

of how these changes occur and how they can be controlled or modified.

Therapy for hyaline membrane disease should be improved by development of new devices and approaches and ways to initiate treatment as soon as possible. The efficacy of present methods of treatment needs to be assessed and knowledge about such methods widely disseminated.

We also need to find out whether bronchiolitis in childhood predisposes to chronic lung disease in the adult.

Actions. To meet these needs in pediatric pulmonary disease and to take advantage of new opportunities developed by research, the Institute will:

1. Extend interdisciplinary studies of biochemical changes associated with hyaline membrane disease through Specialized Centers of Research. In addition, programs will be initiated to study the biochemical changes associated with the development of cystic fibrosis.

2. Develop education programs described in the section on Prevention, Control and Education Programs.

3. Improve management and therapy of hyaline membrane disease through the development of emergency services for rapid transfer of infants with this disease to intensive care units. Programs will be initiated for research and development of new or improved devices for treatment and controlled clinical trials of available methods of treating hyaline membrane disease and cystic fibrosis.

4. Initiate epidemiologic studies to determine prospectively the long-term effects of bronchiolitis in childhood on the occurrence of chronic lung disease in the adult.

Schedule. Present programs in pediatric pulmonary diseases that are not addressed to topics included in the above actions will be terminated or reduced in FY 74, with further reduction in FY 79. Studies relating to pulmonary function in cystic fibrosis and intravenous nutritional support in patients with hyaline membrane disease will be concluded.

Continuing and new actions related to pediatric pulmonary disease will increase in FY 74 and undergo further increases by FY 79. These actions include steadily increasing activities in therapy and epidemiology; a delayed phase-in of education programs, which thus will be able to capitalize on information accruing from other new actions; and increasing programs on hyaline membrane disease and cystic fibrosis through FY 75, followed by a reduction and plateauing in the level of these activities.

EMPHYSEMA AND CHRONIC BRONCHITIS

Program Goals. Research on emphysema and chronic bronchitis, which has focused chiefly on pathophysiology and pulmonary function testing, has not provided the needed information on disease etiology, despite considerable gains in our ability to diagnose disease.

Association of these diseases with certain risk factors, such as cigarette smoking, and in some cases with genetic determinants (e.g., $alpha_1$-antitrypsin deficiency) is strongly suggested. Furthermore, it is now believed that early abnormalities (physiologic, biochemical, etc.) related to emphysema and chronic bronchitis may be detected at a stage when lung damage is still reversible.

- Because of the nature of these disease problems, a goal of the program is to prevent development of these diseases by early diagnosis and identification and control of risk factors.

- At the same time, because of the great number of individuals suffering from already established and progressive disease, another goal is to improve treatment and rehabilitation programs.

- To understand the mechanisms and causes of these diseases is also an important goal and will be greatly aided by the development of basic knowledge of normal lung biochemistry, metabolism, response to injury and repair processes (see the section on Structure and Function of the Lung).

These program goals are established in accordance with the recommendations of the Lung Diseases Panel, the Panel Chairmen, and the National Heart and Lung Advisory Council.

Opportunities and Needs. Among presently identified risk factors, smoking plays a key role in the development of both chronic bronchitis and emphysema. We need to identify the factors in cigarette smoke that

produce lung damage as a step toward reducing the injurious effects of tobacco on the lung. To understand the role of smoking, it is essential to study the mechanisms by which the lung clears itself of particles that are inhaled in cigarette smoke, how these mechanisms are modified by pollutants in the environment, and, through prospective epidemiologic studies, what determines individual differences in response to the harmful effects of tobacco. It is also important for us to investigate measures that will modify the smoking habits of the population. The Panel Chairmen strongly urge that programs be implemented to decrease smoking, particularly in the young.

Host factors, some genetic in origin, may be determinants of emphysema and chronic bronchitis. The association of inherited alpha$_1$-antitrypsin deficiency and the occurrence of emphysema suggests that other situations associated with accelerated enzymatic digestion of lung connective tissue may be implicated in emphysema. A systematic search for inherited enzyme abnormalities that predispose to development of obstructive lung disease is an essential part of a program on host factors.

We need to develop improved techniques and devices to detect biochemical, immunologic or physiologic abnormalities associated with emphysema and chronic bronchitis sufficiently early to effect reversal of the process, something now believed possible. If successfully developed, the next step would be testing such techniques for applicability in mass screening programs. Knowledge of risk and host factors and their control will be essential to successful intervention in the disease process. There is also a need for systematic evaluation of improved therapeutic and rehabilitative approaches.

Actions. To meet these research needs in emphysema and bronchitis and to explore opportunities for solutions, the Institute will:

1. **Develop a multidisciplinary program addressed to the problem of smoking. This program will include investigation of the mechanisms and agents responsible for cigarette smoke injury in emphysema and chronic bronchitis, as well as efforts to modify smoking habits by means of psychological and pharmacological approaches.**

2. **Elucidate the role of host factors, including genetic ones, in the development of emphysema and chronic bronchitis by conducting and extending epidemiological studies.**

3. **Enlarge efforts in emphysema and chronic bronchitis prevention through the development of improved techniques and devices for early detection of reversible diseases and application of new knowledge from studies of risk factors and their control. Epidemiologic screening studies may be required at a later date if this program proves successful.**

4. **Initiate controlled clinical trials to evaluate the efficacy of current and newly developed approaches to therapy and rehabilitation.**

Schedule. Present programs relating to pathophysiology and to diagnosis of advanced disease will be reduced in FY 74 and further by FY 79. Continuing and new actions in emphysema and chronic bronchitis research will be increased steadily. New activities in early diagnosis, clinical trials, and multidisciplinary approaches to smoking reflect increased efforts through FY 79. Host factor research will decrease in FY 76 as prior programs on alpha$_1$-antitrypsin are concluded. As new information on other host factors becomes available, this program approach will increase in activity again in FY 78.

FIBROTIC AND IMMUNOLOGIC LUNG DISEASES

Program Goals. Fibrotic and immunologic lung diseases are induced by external agents that can be prevented or treated by removal of the offending substances or suppression of their effects. Therefore, a primary goal of the National Program in this area is to disseminate information about the causes of these diseases and how to avoid them (see section on Prevention, Control and Education Programs).

In cases where exposure cannot be avoided or the disease prevented, effective treatment depends on understanding the processes leading to disease.

- The research goal is to conduct fundamental investigations essential to the development of improved therapy.

Opportunities and Needs. Where population groups are known to have a high prevalence of pulmonary fibrosis or immunologic lung diseases, epidemiological studies should be carried out to identify the factors responsible. This identification of specific etiological agents is crucial to the development of effective control measures aimed at eliminating these factors.

Advances in biochemistry, pharmacology and immunology, have not yet been brought to bear on problems of lung disease to any degree. These basic scientific disciplines need to be brought into the development of therapy, prevention and control of immunologic and fibrotic lung diseases.

As noted by the Lung Diseases Panel, we need to develop fundamental research on the mechanisms of collagen synthesis and degradation in order to develop therapy directed at specific events in the chain of metabolic events leading to disease.

Many animal models of immunologic and fibrotic lung diseases are available and represent opportunities for study of the pathogenesis of these diseases.

Actions. To meet the needs in fibrotic and immunologic lung diseases and to explore opportunities for solutions, the Institute will:

1. Seek new information about the synthesis and degradation of collagen and the immunologic responses and defense mechanisms of the lung through continued and extended multidisciplinary programs. These will involve collaboration by immunologists, biochemists, physicians and physiologists.

2. Initiate programs to develop pharmacologic agents that will modify the alterations in connective tissue metabolism that lead to pulmonary fibrosis, and study the use of immunologic techniques to stimulate tissue defense mechanisms against immunologic lung diseases.

3. Initiate epidemiologic studies to investigate etiologic factors in population groups characterized by unusual prevalence of fibrotic and immunologic lung diseases.

4. Develop a program of education as discussed in the section on Prevention, Control and Education Programs.

Schedule. Present programs relating to fibrotic and immunologic lung diseases represent miscellaneous activities that are necessary to a balanced effort and therefore will continue.

By redirecting funds from other program areas, both new actions and the total program in fibrotic and immunologic lung diseases will approximately double between FY 74 and FY 79. All of the action areas—multidisciplinary approaches, targeted programs, etiology and epidemiology—reflect incremental activity between FY 74 and FY 79.

RESPIRATORY FAILURE

Program Goals. Respiratory failure may occur in many different disorders, both acute and chronic, pulmonary and nonpulmonary. Considerable progress has been made in the development of sophisticated therapy, but unless treatment is initiated promptly by experienced professional and auxiliary personnel, respiratory failure may lead to death in more than half of those affected. This urgency is particularly noted by the National Heart and Lung Advisory Council members who emphasize in their report early detection and demonstration of emergency services. In many cases of severe injury, the changes that signal the onset of respiratory failure (shock lung) are not detected early enough. The first goal of the National Program in this area is to disseminate the knowledge needed to save lives through early recognition and treatment of respiratory failure (see section on Prevention, Control and Education Programs).

- The research goal is to develop modes of therapy that are less costly, less complicated to administer, and more readily available than those now in use for respiratory failure.

- Another goal is to apply new technology to the treatment of respiratory failure, and to develop improved diagnostic, monitoring and rehabilitation devices and techniques.

Opportunities and Needs. We need to evaluate critically current devices and techniques for treatment of respiratory failure, for immediate efficacy as well as for long-term effects. New devices that can be easily used by physicians and allied health personnel need to be developed to provide more effective treatment. As new devices and techniques are developed, their efficacy must be tested in controlled clinical trials.

Actions. To deal with the problems of respiratory failure or impaired lung function, the Institute will:

1. Expand programs addressed to ventilatory assist devices and oxygenators to insure improvements in available devices and development of new ones. Presently available and promising new devices will be tested in controlled clinical studies. Emergency medical services will be developed to

insure the early initiation of treatment. Specialized Centers of Research where sophisticated techniques and experienced professional personnel are available will be continued and extended in order to capitalize on what is known and to improve present modes of therapy.

2. **Initiate development of devices and techniques for monitoring of respiratory function and efficiency in patients with impaired lungs.**

3. **Develop and test improved invasive and noninvasive instruments for blood and respiratory gas analysis in patients with lung disease.**

4. **Develop devices and techniques to detect and monitor small airway resistance and structural and functional abnormalities of diseased lung (see section on Emphysema and Chronic Bronchitis).**

5. **Initiate demonstration projects to disseminate available information (see section on Prevention, Control and Education Programs).**

Schedule. Certain present programs relating to respiratory failure will be completed. These include studies relating to diagnosis of manifest pulmonary failure, serial monitoring and physiology. Continuing and new actions on new methods of therapy and improved devices for support of lung function and for diagnosis of lung diseases will be increased gradually through FY 79.

BLOOD DISEASES AND BLOOD RESOURCES

The Institute's plan for a program against blood diseases and the problems of blood resources is described in this section.

It draws upon the recommendations of the Blood Diseases and Blood Resources Panels, the Panel Chairmen, and the National Heart and Lung Advisory Council. It is responsive to the Legislation which specifically requires, "studies and research into blood diseases and blood, and into the use of blood for clinical purposes and all aspects of the management of its resources in this country . . . ."

The blood programs of the National Heart and Lung Institute deal with three problems: Bleeding and Clotting Disorders, Sickle Cell Disease and Related Disorders of the Red Blood Cell, and Blood Resources. These problems are defined above in Section II, The Problems.

BLEEDING AND CLOTTING DISORDERS

As discussed above in Section II, bleeding and clotting disorders are closely related. The major problems addressed by the National Program in this area are: The Hemophilias, Platelet Abnormalities, Microcirculatory Thrombosis, Thromboembolism in Relation to Prosthetic Devices, and Thromboembolic Disorders.

The Hemophilias

Program Goals. The hemophilias represent striking examples of diseases in which basic and clinical research have led to advances that have revolutionized patient care. Laboratory research in the 1950's and 60's first provided conclusive evidence that what appeared genetically and clinically to be a single disease in actuality resulted from a deficient activity of either one of two different clotting proteins (called factors VIII and IX) which are entirely different.

- A major research goal of the hemophilia program is to improve the methods for preparing the missing factors so that they can be made available to all who need them at reasonable cost.

A second goal is the education of the public which is discussed in the section on Prevention, Control and Education Programs.

Opportunities and Needs. The Blood Diseases Panel, the Panel Chairmen, and the National Heart and Lung Advisory Council all urge that a strong and positive program of genetic research and counseling in hemophilia be established.

We know how to extract the clotting factors from the plasma of human blood donors, but not how to do it cheaply or efficiently. We need to improve methods for producing the factors, systematize treatment schedules, and reduce costs through home therapy programs. The Panel Chairmen recommend that methods be improved for harvesting, concentrating and storing these factors. The feasibility of prenatal diagnosis for preventing the disease needs to be pursued. Molecular or cellular manipulations to produce the missing activity, and tissue transplantation, appear realistic objectives for eliminating the disease in the future.

Actions. To meet these needs and to explore the opportunities, the Institute will:

1. Support studies in coagulation and hemophilia, and apply the resultant information to treatment and to new approaches for cure and prevention.

2. Support studies to improve methods for harvesting, concentrating and storing these factors.

3. Carry out clinical trials of various treatment schedules.

4. Develop information, education and genetic counseling services as discussed in the section on Prevention, Control and Education Programs.

5. Establish up to three Specialized Centers of Research for the bleeding disorders. Such centers will include skilled specialists, experienced in dealing with all aspects of the care of hemophilic patients, who will organize and support home care programs; educate the hemophilic patient in all aspects of his disease; provide support to his family in making necessary social and psychological adjustments; conduct clinical research trials on promising new preparations; and educate health personnel in the care of hemophilic patients.

Schedule. Current research programs will be completed by FY 78, while grant activities for acquisition of new knowledge will be increased annually between FY 74 and FY 78. New centers will be established and their support will peak in FY 76 and FY 77. Controlled trials of treatment schedules will be concluded in FY 78.

Platelet Abnormalities

Program Goals. In the mid 1960's, new interest developed in the role of blood platelets. Today, rapid progress is being made in this area. Recent studies suggest a broad biologic role for platelets including involvement in disorders of the microcirculation, in the development of atherosclerosis, and in certain types of host-defense reactions. Nevertheless, details of their functions and how they can be manipulated to benefit the patient remain poorly understood. The recommendations of the Blood Diseases Panel strongly center on the determination of the role of platelets and the mechanisms and effects of platelet abnormalities.

- The goal of this program is to determine the role of platelets in thrombosis and hemorrhage.

Opportunities and Needs. The hypothesis that modifying platelet function by such relatively harmless drugs as aspirin will reduce the incidence of myocardial infarction is of major interest. We have advanced to the point where it is now of the highest urgency to conduct controlled clinical trials in high risk patients to test this hypothesis. Indeed, the Panel Chairmen in their report give high priority to conducting such clinical trials in patients with coronary heart disease and cerebral vascular disease. While these trials will be expensive, the potential payoff is enormous.

Actions. To meet these needs and to take advantage of the opportunities, the Institute will:

1. Conduct clinical trials of drugs which inhibit platelet aggregation in patients at high risk from vaso-occlusive disease such as myocardial infarction and postoperative pulmonary embolism.

2. Support the acquisition of further knowledge regarding platelet function, ultrastructure, and the interaction of platelets with the vessel lining.

Schedule. Continuing and new actions will be increased for basic research on platelet function and for therapeutic trials with drugs that inhibit platelet aggregation.

Microcirculatory Thrombosis

Program Goals. As indicated earlier, bleeding and clotting within the microcirculation play a role in many disease states. Consequently, improved understanding of the microcirculation offers an enormous opportunity for better health maintenance.

- The goal of this program is to understand better the microcirculation and the systemic effects of bleeding and clotting within this system.

Opportunities and Needs. Very much more remains to be learned about the microcirculation and its role in vascular perfusion and permeability in clinical disorders. For instance, microcirculatory hypoperfusion has been implicated as the focal point of shock. The muscle cells in the walls of the microcirculatory vessels are extremely sensitive to chemical stimuli, so sensitive that they respond to as little as one hundredth the amount of substance required to constrict or dilate a large blood vessel. This sensitivity contributes to the independent behavior of the microcirculation. A quantity of a chemical sufficient to cause dramatic

changes in the microcirculation simply has no effect on the larger vessels. The Blood Diseases Panel recommends specific projects to examine various factors and evaluate the mechanisms of the microcirculation. We need to understand the factors responsible for bleeding and clotting within the microcirculation, develop methods to prevent and possibly reverse these derangements, and improve the techniques for diagnosing, measuring, and monitoring disorders of the microcirculation.

Actions. To meet these needs and to explore the opportunities, the Institute will:

1. **Support the development of techniques which provide greater reliability, specificity, sensitivity and simplicity in detecting microcirculatory bleeding and clotting.**

2. **Encourage studies on the properties and functions of the microcirculation, particularly the wall of the microcirculatory vessels, and the relationship of these to bleeding and clotting and various disease states.**

Schedule. The present commitment for research activities in microcirculation will be completed by FY 78. New activities will be developed and receive increasing annual support between FY 74 and FY 79.

Thromboembolism in Relation to Prosthetic Devices

Program Goals. The only truly nonthrombogenic (clot-resisting) material known today is the lining of normal blood vessels. The development of nonthrombogenic artificial materials requires special emphasis because such surfaces would provide the key to the development of a whole range of diagnostic and therapeutic devices. At present, artificial devices can be used only if the period of contact with the blood is short; if their surface area is very small, as with heart valves; if the risk of thrombosis is accepted, as in vessel grafts; if the surfaces are constantly washed clean in areas of high fluid flow, such as intra-aortic balloons; or if their use is supplemented by drugs that inhibit clot formation, such as heparin in cardiopulmonary bypass or in hemodialysis. Because no truly nonthrombogenic artificial materials are available today, the impressive surgical advances in replacement of sections of diseased blood vessels and heart valves and production of functioning artificial kidneys and heart-lung machines cannot be fully exploited. The Blood Diseases Panel and the National Heart and Lung Advisory Council encourage basic research studies to understand surface characteristics of biomaterials designed for contact with the blood.

- The goal of this program is to study the blood vessel lining, hematology and hemodynamics, and to develop nonthrombogenic materials, both living and nonliving, suitable for use in prosthetic devices.

Opportunities and Needs. We need to know why healthy blood vessel lining keeps blood from clotting on contact, how blood components interact with the vessel wall, and how the dynamics of blood flow affect clot formation. Because of the nature and complexities of these interactions, solutions will require close collaboration by organic and polymer chemists, biochemists, clinical and research hematologists and surgeons. Important and promising leads already exist for the development of materials having long-term compatibility with the blood.

Actions. In accordance with these goals, opportunities and needs, the Institute will:

1. **Expand research and development efforts on materials for use in prosthetic devices in contact with blood involving the support of synthesis, fabrication, and evaluation of new polymeric, metallic and ceramic biomaterials.**

2. **Implement further research on development of pseudo and normal intimal surfaces on blood pumps and other cardiovascular devices.**

3. **Develop improved means for screening biomaterials and characterizing their behavior prior to clinical use.**

4. **Initiate development of instrumentation for detecting blood clots on prosthetic devices, and coronary and cerebral arteries and other blood vessels.**

5. **Develop and test assay techniques for determination of molecular and cellular changes in blood cellular components, proteins and enzymes.**

Schedule. Present research programs will be completed by FY 78, while new research actions will receive increasing annual support between FY 74 and FY 79. Collaborative research projects will be initiated in FY

75, increase in FY 76, and continue at a reduced support level until FY 79.

Thromboembolic Disorders

Program Goals. The approaches to both venous and arterial thromboembolism share two important concepts: (1) their causes involve an interplay of the blood coagulation system, the platelets, the vessel lining and the properties of flowing blood, and (2) application of previously accumulated and newly generated knowledge in these areas can be expected to provide health benefits to a large number of American people.

- The goal of this program is to facilitate detection and treatment of thromboembolic disorders by development of techniques and evaluation of drugs.

Opportunities and Needs. Because these disorders have much in common, they can be categorized together. We urgently need methods for detecting minimal damage or obstruction in arteries and veins before symptoms appear; evaluation of clot-preventing or clot-dissolving drugs in the prevention and treatment of thrombosis and embolism in high risk patients, and much more information about the role of thrombosis in myocardial and cerebral infarction. The Blood Diseases Panel recommends specifically that risk factors for arterial and venous thromboembolism be identified so that they may be prevented, and the National Heart and Lung Advisory Council generally urges the study of the mechanism of thrombosis and the performance of clinical trials of promising new antithrombotic drugs.

Actions. To meet these needs and to take advantage of research opportunities, the Institute will:

1. **Initiate development programs to evaluate and compare noninvasive techniques which hold promise for early detection.**

2. **Conduct controlled clinical trials of clot-preventing and clot-dissolving drugs in individuals at high risk from venous thromboembolism, and also in patients with arterial disease and actual or impending myocardial infarction.**

3. **Encourage research on atherosclerosis and thrombosis and on their interrelationships.**

4. **Establish a national or international registry to assess the degree of atherosclerosis and thrombosis (especially of arteries of the heart and brain) among autopsied patients who had known abnormalities in clotting proteins, platelets, or clot-dissolving (fibrinolytic) enzymes.**

5. **Develop colonies of animals with specific abnormalities in clotting proteins, platelets, and fibrinolytic enzymes for use in research. This will include primate colonies for the study of the interrelationships of atherosclerosis and thrombosis.**

Schedule. Present programs will be completed in FY 78. Basic research in clotting will receive increased support between FY 74 and FY 78. Trials of antithrombotic drugs and studies of methods for early diagnosis of thrombosis will receive additional support, with the former peaking in FY 77.

SICKLE CELL DISEASE AND RELATED DISORDERS OF THE RED BLOOD CELL

The three groups of disorders considered in this section include Sickle Cell Anemia and Sickle Cell Trait, conditions resulting from abnormal hemoglobins closely related to sickle cell hemoglobin, such as Cooley's Anemia, and defects affecting the Red Blood Cell Membrane and Enzyme Systems.

Sickle Cell Anemia and Sickle Cell Trait

Program Goals. The research goals of the sickle cell disease program are to:

- Develop improved therapy for sickle cell crises; increase knowledge of the fundamental biology of the disease and its complications; and develop effective and acceptable methods for screening and counseling.

The goal of education of the public and the medical profession is discussed in the section on Prevention, Control and Education Programs.

Opportunities and Needs. Despite knowledge of the precise defect in the sickle hemoglobin molecule, the areas of ignorance regarding sickle cell disease are greater than the areas of understanding. Therefore, a balanced program must address a variety of problems, from understanding of the red cell to treatment of the patient and education of the community.

The biology of the red cell, the mechanisms of sickling, the effects of combinations of sickle hemoglobin and other abnormal hemoglobins, the effect on the red cell of compounds that may prevent or reverse sickling are some of the problems that must be addressed to gain the knowledge necessary for rational therapy.

We must continue to search for therapeutic measures that are effective, safe and simple. As promising therapies are developed, they must be tested in clinical trials. Better screening techniques need to be developed to detect hemoglobin variants including sickle hemoglobin. We need simple, rapid, accurate and reliable methods suitable for mass screening.

Effective community programs of screening, education and counseling need to be demonstrated in a variety of community settings. The advice of the Blood Diseases Panel, the Panel Chairmen and the National Heart and Lung Advisory Council places special emphases on these programs.

The greatest need is for dissemination of accurate information and for education of the public regarding the meaning of sickle cell trait and sickle cell anemia (see section on Prevention, Control and Education Programs).

Actions. To meet these needs and to take advantage of new opportunities to solve these problems, the Institute will:

1. **Continue emphasis on the National Sickle Cell Disease Program initiated in 1971. Basic and clinical research, clinical application, clinical trials, training and education and efforts in screening, counseling, rehabilitation and information dissemination will be increased.**

2. **Expand studies to understand better the molecular structure of sickle hemoglobin, interactions of other abnormal hemoglobins with sickle hemoglobin, differences in flow patterns between normal and sickle red cells, and the effect of various agents on all of these.**

3. **Implement development and testing of devices for mass screening and diagnostic testing of hemoglobin abnormalities in patients with sickle cell, Cooley's anemia, and other related blood diseases.**

4. **Continue to develop interfaces with other institutes of the National Institutes of Health and other federal agencies: National Institute of Arthritis, Metabolism, and Digestive Diseases; National Institute of General Medical Sciences; Health Services and Mental Health Administration; Department of Defense; Department of Labor; and Veterans Administration.**

Schedule. In FY 74, sickle cell disease programs will be expanded and increased emphasis will be placed on control, including information, education and demonstration as discussed later in the section on Prevention, Control and Education Programs. No programs are scheduled for completion during this early phase.

Cooley's Anemia and Related Hemoglobin Variants

Program Goals. The goals of the research programs on Cooley's anemia are to:

- Develop a simple screening technique to identify carriers and to determine the prevalence of the disease; develop improved treatment methods, preferably ones that would obviate the need for frequent transfusion; and increase fundamental knowledge regarding control of synthesis of the hemoglobin molecule with a view toward achievement of preventive measures.

Opportunities and Needs. We know a considerable amount about the molecular abnormality in Cooley's anemia, but we do not know how to correct it. Present treatment is limited to frequent transfusions. While this gives temporary relief from the anemia, it burdens the body with excess iron that cannot be eliminated. Development of a substance, free of serious side effects, that would be effective in reducing the iron overload, would prolong the life of patients with Cooley's anemia. The Blood Diseases Panel recommends the collection of data on the natural history of Cooley's anemia and the improvement of methods for eliminating iron. A rational basis for therapy will depend upon further understanding of events at the molecular level; therefore, fundamental research must be continued.

We presently have no simple method for screening for Cooley's anemia trait and, therefore, no way of identifying carriers. Such a technique needs to be developed.

Actions. To meet these needs and to explore these opportunities, the Institute will:

1. Continue its efforts in Cooley's anemia in coordination with other institutes at the National Institutes of Health and with other federal agencies. These programs will include studies on the mechanism of hemoglobin synthesis, clinical research to determine the effect of splenectomy (removal of the spleen) and transfusion programs on the course of the disease, development of agents for removal of excess iron, prenatal diagnostic approaches, and better laboratory methods for detecting the carrier state.

2. Evaluate education methods and develop counseling programs as described in the section on Prevention, Control and Education Programs.

3. Encourage the establishment of reference laboratories for the diagnosis and investigation of hemoglobin variants.

Schedule. Most of the Institute's intramural program in blood diseases is directly concerned with the acquisition of fundamental knowledge in Cooley's anemia and sickle cell anemia. The two diseases are inseparably linked at the fundamental level and programs will be continued jointly. The programs for research in Cooley's anemia and related red blood cell disorders will be expanded gradually until FY 79.

Red Blood Cell Membrane and Enzyme Systems

Program Goals. Compared with other body cells, red blood cells are easily obtained and readily studied. Their metabolism is complex and specialized; yet, it is simple compared with the metabolism of other body cells and shares enough common features to serve as a useful model. Thus, clues obtained in red blood cells regarding metabolic controls and regulation may be expected to have wide applicability for understanding other, less accessible, body cells.

- The goal of this program is to learn as much as possible about membrane structure and function and intracellular metabolic activity. Such knowledge will contribute toward control, treatment, and prevention of the specific diseases. High yields in all of medicine can be expected from application of this knowledge to other, inaccessible cell systems.

Opportunities and Needs. Because most red cell enzyme disorders, except G6PD deficiency, are rare, it is inefficient and wasteful for every hospital laboratory to diagnose and investigate them. Several reference laboratories need to be established to perform these functions. The Blood Diseases Panel calls for the support of such regional laboratories.

The mechanism of the anemia resulting from the interaction of drugs with G6PD-deficient red cells requires further study.

Actions. To explore these needs and opportunities, the Institute will, in coordination with the National Institute of Arthritis, Metabolism and Digestive Diseases:

1. Continue to support research on normal and abnormal red cell metabolism, membrane structure and function.

2. Encourage the establishment of reference laboratories for the diagnosis and investigation of red cell enzyme and membrane disorders as mentioned above in the section on Cooley's anemia, Action 3.

Schedule. These activities will be expanded gradually under the grant mechanism and in conjunction with investigator-initiated work in Cooley's anemia and related hemoglobin variants.

BLOOD RESOURCES

Scientific advances must be applied to increase the quality and number of blood products available. Managing the national blood resource requires a combination of human resources, sociologic, economic, scientific, medical, and management expertise, and technology, instrumentation and manufacturing capabilities.

Four program areas are discussed in this section: a Nationwide Blood System; Safety of Blood Therapy; Blood Component Therapy; and Transplantation Biology. These four areas are discussed in terms of their opportunities, needs, and actions. One action, the development of Specialized Centers of Research, is applicable to all the program areas. This action, together with an overall schedule for the entire blood resources program, is discussed last under Overall Action and Schedule. The program goals are also applicable to all

program areas and are discussed first as Overall Program Goals.

Overall Program Goals

The blood service complex has provided essential services and products; it has not consistently maintained an adequate supply or achieved the highest attainable quality of blood therapy.

- The goal of this program is to achieve an adequate supply of high quality blood and blood components by utilizing the national blood resource with maximal efficiency, economy and safety.

Management of the nation's blood resources was addressed by the Blood Resources Panel and the National Heart and Lung Advisory Council, and this has been considered in developing the Institute's recommendations.

Nationwide Blood System

Opportunities and Needs. The present complex by which blood and blood products are provided to the American people is fragmented, inadequately regulated, unplanned and poorly managed. The result is inefficient use of resources and a compromise in quality and safety. What is known often has been applied slowly and sometimes not at all. Despite these serious shortcomings, the complex has enormous strengths and, in the main, has served the American people well. Present needs are to:

- Develop and promulgate a National Blood Policy which establishes the goals of a nationwide blood system, specifies the steps to achieve these goals, and provides a framework for building a pluralistic system, relying on existing resources whenever possible

- Establish data and information systems on all aspects of blood banking, including cost-charge relationships, in order to evaluate the performance of the system and to design necessary changes therein

- Employ the full regulatory authority of the Food and Drug Administration to enhance the quality and effectiveness of the national blood supply.

Actions. To achieve the goal of an improved national blood system will require collaboration and cooperation among a number of agencies, public and private. The Institute will:

1. Facilitate, in conjunction with the Bureau of Biologics of the Food and Drug Administration, and other agencies, coordination of private and public organizations involved in blood banking with a primary goal of creating an all-voluntary blood donation system, and regional integration to increase effectiveness.

2. Create a Federal Blood Data Collection Center, in cooperation with the Bureau of Biologics and the Department of Commerce, to provide comprehensive and continuous information concerning the nation's blood supply, its size, distribution and use.

3. Identify and describe key operational aspects of the American blood system; study the applicability of automated methods for tracking blood inventories; develop methods for predicting blood needs; implement new incentives for blood donation; devise methods for utilizing more effectively the present donor pool; and expedite the clinical application of new developments in blood procurement and distribution.

Safety of Blood Therapy

Opportunities and Needs. In spite of rapid advances in the understanding of hepatitis, including serum hepatitis, there is still no way to ensure that blood from a given donor will not transmit the disease. Cytomegalovirus disease is also emerging as a major cause of death in transfused patients whose immune mechanisms are depressed. The role of the blood donor in transmitting cytomegalovirus must be elucidated, and means of prevention developed and implemented. Histocompatibility antigens transfused in blood may make further transfusions useless if the recipient becomes sensitized to them. Means of removing such antigens need to be developed. Human error in matching donor and recipient remains a major hazard in transfusion therapy and fail-safe systems need to be developed and applied.

If human error is eliminated, retransfusing the patient's own blood constitutes the safest form of transfusion therapy. Means to develop further this form of therapy, termed autotransfusion, both by having the patient bank his blood prior to need, and returning blood lost during surgery to him, must be explored. In addition to increasing safety, this form of therapy might be expected to reduce significantly the demand on the nation's blood resources.

Actions. The Institute will:

1. Participate with other agencies in a concerted attack on hepatitis which will include development and use of more sensitive and practical tests for detecting carriers, studies of the carrier state, and development of methods for passive and active immunization.

2. Support studies to eliminate the transmission of cytomegalovirus disease.

3. Develop fail-safe systems for donor-recipient identification.

4. Explore efforts to increase the use of autotransfusion.

Blood Component Therapy

Opportunities and Needs. The medical demand for red blood cells, as distinguished from other blood components, sets the pace for the collection of whole blood. Patients who need red cells often do not need the other components. Currently, whole blood is used in more than three-fourths of all transfusions; experts indicate that whole blood is needed in less than one-fourth of cases. Reducing the use of whole blood not only constitutes good medical practice, but increases the availability of components often in short supply and needed by others. For example, factor VIII and factor IX concentrates are needed to control hemorrhage in hemophilia; gamma globulin can prevent many infectious diseases even if given after exposure; platelets can restore the ability to clot if the patient's platelet production is impaired. Optimal utilization of the nation's blood resource requires:

- Better methods of blood cell separation and preservation and of plasma fractionation so that the many important components can be recovered efficiently and economically
- Clearer indications for the use of individual components and better methods to assess their effectiveness.

It also requires ways to educate the physician regarding optimal use of blood components to moderate his demands on the nation's blood resource. This is discussed further in the section on Prevention, Control and Education Programs.

Actions. The Institute will:

1. Support basic and applied research to improve methods for storage and preservation of blood cells, for collecting blood without traumatizing cellular and molecular components, for maintaining viability and function of platelets and white blood cells, for expediting development of agents which stimulate formation of blood cells, for making fractionation of blood more efficient and less expensive to assure adequate amounts of human coagulation factors, particularly factor VIII for hemophilia, and for devising methods to cope with the newly emerging demands on blood resources.

2. Develop means to enhance and evaluate the appropriateness of blood utilization through clearer indications for the use of blood components and better methods to assess their effectiveness.

3. Support education programs regarding optimal use of blood components as described in the section on Prevention, Control and Education Programs.

Transplantation Biology

Opportunities and Needs. In addition to handling blood, a nationwide blood system could also be responsible for the preservation, storage, and typing of tissues and organs for transplantation. Fundamental knowledge in transplantation biology will be necessary before transplantation can be used more widely and more successfully. Simultaneously, we need to develop better means for managing the transplant patient, to design a system of organ procurement on a regional and national basis, and to resolve the ethical, legal and moral questions involved.

Actions. The Institute will:

1. **Encourage fundamental research (in conjunction with other Institutes), in immunology, immunogenetics, and other aspects of transplantation biology.**

2. **Initiate clinical studies, (in conjunction with other Institutes) to improve the management of the post-transplant state, such as prevention of graft-versus-host reaction, the development of better immunosuppressive techniques, and the prevention and treatment of infection.**

3. **Encourage efforts to develop a system of organ procurement on a regional and national basis.**

4. **Implement studies to improve organ preservation devices.**

5. **Promote public dialogue on the ethical, moral and legal problems associated with organ transplantation.**

Overall Action and Schedule

Action. Applicable to all of the above blood resource problems are Specialized Centers of Research. The NHLI concurs with the Blood Resources Panel report, the Panel Chairmen's report and the recommendations of the National Heart and Lung Advisory Council that the above programs could be substantially aided by activating one or two centers in Blood and Blood Resources on a pilot basis. These centers will emphasize improved therapy using blood cells, particularly white cells and platelets, and plasma protein components including those used in treatment of hemophilia, and will contain pilot plants to develop and test new methods for plasma fractionation. Studies on hepatitis could be coordinated in these centers. The program could also aim at acquisition of additional knowledge fundamental to successful tissue and organ transplantation.

Schedule. Present programs in blood and blood resources which have achieved their objective will be terminated and replaced by the programs identified above. The total activities in blood resources will be increased gradually over the next five years and approximately double by FY 79.

PREVENTION, CONTROL AND EDUCATION PROGRAMS

Prevention of heart and blood vessel, lung and blood diseases will require not only the acquisition of new knowledge through research programs but also the demonstration to the medical profession and the public of the applicability of this knowledge. Further, prevention will require local community and regional participation in the control of these diseases.

The Legislation specifically directs the National Heart and Lung Institute to establish cooperative programs with nonfederal health agencies for the purpose of controlling, and in the long-term, preventing these diseases. The four advisory Panels recommend the establishment of such programs for many of the specific disease problems. The National Heart and Lung Advisory Council recommends to the Institute that demonstration projects be developed to test education methods, to develop community and regional efforts for detection, diagnosis and treatment of disease and for rehabilitation, and to demonstrate to the public the clinical applicability of research methods. The members emphasized that these projects be specific, be time-limited, be reported in the media, and that they be conducted in cooperation with existing local health resources to facilitate the transition from federal support of demonstration to local control of disease.

We believe that demonstration and control programs will help to effect the transmission of fundamental research advances to the public and thereby help to promote the health of our citizens. These programs are an essential link between biomedical research and health care.

- The overall goal of the prevention and control programs is to benefit the citizens of our country by demonstrating to the practicing medical profession and the public means to promote health, prevent disease, treat disease, and restore health.

A major program effort is also required to disseminate information and to educate the public about these disease problems. Public awareness and access to current information are fundamental to the prevention

and control of many specific diseases. It has been demonstrated that early recognition and treatment of heart problems are significant in preventing serious complications and death; that awareness of environmental factors and motivation to do something about them may be effective in preventing pulmonary diseases; and, that knowledge of carrier status enables individuals to make informed choices regarding transmission of genetic blood abnormalities. Similarly, information and education about the nation's blood resources will be essential in our efforts to motivate individuals to donate blood.

The professional community—research scientists, physicians, and related health personnel—also require current and up-to-date information about these disease areas. Many action programs outlined in the NHLI Program Plan call for multidisciplinary collaboration; exchange of information across fields of specialization will be necessary to fulfill many of our goals. Information about new techniques and methods, drugs and devices will facilitate the flow of research into application and treatment.

The Legislation requires that the Director of the NHLI appoint an Assistant Director for Health Information Programs. This person will direct information and education programs. The Act also directs the Institute to develop programs for "public and professional education relating to all aspects of such diseases and the use of blood and blood products and the management of blood resources." The four advisory Panels and the National Heart and Lung Advisory Council also have emphasized repeatedly in their discussions the need for information and education programs.

The NHLI has many activities and programs that relate directly to education and information. Traditionally, the NHLI has made available to the public brochures, pamphlets and booklets on various heart and blood vessel, lung and blood diseases and blood resources. The Institute also has worked closely with the American Heart Association and other voluntary and professional organizations in matters dealing with consumer information and education, to coordinate efforts, avoid needless duplication, and obtain maximum impact. Now, with the added impetus provided by new authorities and responsibilities generated by the Act, the Institute is broadening the scope and intensifying the efforts of its programs in education and information.

The overall goals of the education and information programs are to:

- Make the public aware of the magnitude of these disease problems, the associated risk factors and available methods of therapy
- Keep the health professional community abreast of new information and techniques and, thereby, also to facilitate the flow of modern therapy and information to the public.

Discussed below are specific examples of prevention, control and education programs for the National Program in heart and blood vessel, lung and blood diseases and blood resources. Also presented are overall schedules and actions which are applicable to all the disease problems.

HEART AND BLOOD VESSEL DISEASES

We already have considerable knowledge for the prevention and control of some heart and blood vessel diseases. However, the effective application of this knowledge to individuals most urgently in need of such measures will require more specific research and evaluation efforts. A systematic program to apply existing knowledge in heart and blood vessel diseases will materially reduce disability and death from these diseases.

Particular emphasis should be placed on the testing and evaluation of a program for the prevention of the two major cardiovascular diseases—hypertension and arteriosclerosis. In these diseases, a sufficient base of knowledge exists which could result in substantial reductions in morbidity and mortality if implemented through coordinated, comprehensive programs. Prevention or amelioration of the consequences of other cardiovascular diseases will also require attention in planning the National Program. Specific programs for hypertension, arteriosclerosis, coronary heart disease, and congenital heart disease are discussed in this section.

HYPERTENSION

Program Goals. We know that drug therapy to control blood pressure reduces the incidence of strokes and heart failure among persons with moderate and severe

hypertension. However, only about 12 percent of hypertensives are currently receiving adequate treatment. Immediate efforts to expand current program initiatives through existing medical networks are urgently needed to bring individuals with moderate and severe hypertension under effective treatment. Sustained effective blood pressure management in such persons should result in a reduction of disability and mortality of as much as 40 percent when compared with expected rates for untreated hypertension.

- A national goal of the program is to motivate all adults to have their blood pressure checked annually and for those found to be hypertensive, to urge them to obtain proper therapy.

Opportunities and Needs. Important opportunities and needs in the prevention and control of hypertension include establishment of simplified medical regimens using available hypertensive drugs; development of systems which utilize nurses and allied health professionals to carry out therapeutic regimens under medical supervision; study of ways to motivate patients and to remove barriers to continued adherence to long-term antihypertensive drug therapy; and consideration of using demonstration programs in the community to seek effective methods of implementing hypertension detection, diagnosis, treatment and follow-up systems in cooperation with existing medical and community health resources.

Actions. To meet these needs and to explore these opportunities, the Institute will:

1. Continue the Hypertension Information and Education Program initiated in 1972 to expand public and professional awareness of the dangers of high blood pressure and the benefits of treatment.

2. Direct special effort toward cooperation with existing medical, health and community resources. The methods developed should be applicable for subsequent continuation by the community and adoption by other similar communities.

3. Initiate hypertension prevention and follow-up programs for high risk popuiations to develop, adapt and demonstrate effective prevention of the complications of hypertension in special segments of the population known to have a high rate of prevalence and mortality from hypertension. These include inner city black populations and rural black females. The special health, educational and social problems of these population groups will require the development of new approaches. Assessment of the effectiveness of using allied health personnel from the community to implement these programs, and evaluation of the ability to maintain hypertensives on long-term adequate blood pressure management will be built into the planning of these demonstrations. Knowledge gained from these programs will be reported rapidly so that successful control efforts can be duplicated in other similar populations.

Schedule. The Institute currently has some activity in this area which will be continued with a modest increase in emphasis over the next two to three years.

ARTERIOSCLEROSIS

Program Goals. A number of factors have been identified that increase susceptibility to atherosclerosis and coronary heart disease. These include elevated blood lipids, high blood pressure and cigarette smoking. These risk factors can be modified and the public needs to know how this can be done. Program goals are to:

- Reduce disability and death from arteriosclerotic disease of the blood vessels to the heart, brain and extremities through the prevention and control of risk factors

- Conduct research on improved methods for rehabilitation.

Opportunities and Needs. It is now possible for us to identify persons who may be at increased risk of developing coronary heart disease, stroke or peripheral vascular disease by measuring their blood lipids, blood glucose, blood pressure, weight, and obtaining information on cigarette smoking. An electrocardiogram further improves the prediction of risk.

Using these factors as indicators, we can identify the 20 percent of the population who are most likely to develop 40 percent of the coronary heart attacks, 50 percent of the strokes and 50 percent of the clinical peripheral vascular disease over a subsequent six-year period. This is not an absolute because heart attacks, strokes and peripheral vascular disease also occur in persons without such risk factors. However, the highest priority needs to be given to preventive efforts for those high risk susceptible individuals who are identifiable by relatively simple procedures.

Once susceptible individuals have been identified, measures can be initiated to help these persons reduce their risk factor status through dietary measures, lipid lowering drugs, blood pressure lowering drugs and modification of living patterns. This is a difficult task and how to achieve such changes in an acceptable manner for large segments of the population remains to be determined.

In addition, once a heart attack or other serious cardiac illness has occurred, the rate and completeness of return towards normal functioning in society and enjoyment of life remains inadequate. Present studies show that disability can be minimized and recovery hastened by appropriate attention to medical and psychological factors. However, the optimal, practical methods for achieving such rehabilitation need development, assessment and demonstration.

Actions. To meet these needs and to explore the opportunities, the Institute will:

1. Cooperate with the Department of Agriculture and other federal agencies having a nutrition-related interest to establish policies and education programs on the role of nutrition in heart disease. Nutrition research to develop improved methods for dietary therapy of specific types of hyperlipoproteinemia will also be carried out in the Lipid Research Clinics.

2. Support, in cooperation with the Department of Agriculture and the Food and Drug Administration, a special program to update the information on composition of foods in the American marketplace. A widespread need has been voiced for data on specific nutrients such as fats, fatty acids, sterols, and carbohydrates.

3. Explore, in coordination with the Social and Rehabilitation Service, the feasibility of establishing demonstration programs in rehabilitation of patients with cardiovascular disease.

Schedule. The Information Program for risk factor prevention will be increased in FY 75 and receive sustained support thereafter. It is projected that support for nutrition programs will double in FY 75 and increase incrementally thereafter.

CORONARY HEART DISEASE

Program Goals. As discussed in the Research Program section in Coronary Heart Disease, emergency medical care for the person with suspected heart attack is a major problem, and there are 400,000 deaths from coronary heart disease prior to hospitalization.

- The goal of this control program is to introduce the developments in emergency medical care for the cardiac patient into comprehensive emergency care systems.

Opportunities and Needs. A saving in life and probably a decrease in disability from heart attack can be achieved by improved emergency medical systems for the cardiac patient.

Action. To meet this need, the Institute will:

1. Contribute, in collaboration with other federal agencies, to the design and analysis of the cardiac elements of emergency care in comprehensive emergency medical systems. Such programs will emphasize intensive professional education, development of instrumentation for field use in telemetry, and telemetry in telecommunications.

Schedule. The program is contingent upon scheduling of the comprehensive emergency medical system; NHLI components could be initiated in late FY 74 and continued through FY 77.

CONGENITAL HEART DISEASE

Program Goals. A substantial fraction of the deaths from congenital heart disease occur in the newborn period.

- The goal of this control program is to recognize and manage congenital heart disease in the newborn.

Opportunities and Needs. A substantial saving in lives can be achieved by early recognition of cardiac problems in the newborn.

Action. To meet this need, the Institute will:

1. Explore the feasibility of demonstration programs for the early recognition of cardiac (and respiratory) problems in the newborn. Such programs will emphasize intensive professional education, development of instrumentation for improved detection, better interhospital communication and transport, and the availability of diagnostic and surgical facilities for treating critically ill infants.

Schedule. The program will be initiated in FY 75 and continue through FY 77.

LUNG DISEASES

The major emphasis in prevention, control and education in the lung diseases area will be on smoking control programs to decrease the problems of emphysema and chronic bronchitis. Other efforts include programs in pediatric pulmonary diseases, fibrotic and immunological lung diseases, and respiratory failure.

EMPHYSEMA AND CHRONIC BRONCHITIS

Program Goals. Cigarette smoking is believed to be a prime factor in the etiology or exacerbation of chronic bronchitis and emphysema, and a contributing factor to environmental lung diseases, including pneumoconiosis and hypersensitivity lung diseases. Up to 20 percent of smokers have chronic obstructive lung disease and almost all patients with this disease are smokers. Extensive studies document conclusively that cigarette smokers are far more likely to develop emphysema than non-smokers. Also, once developed, it progresses much more swiftly in those who smoke. Repeated exposure to pollutants in the air also contributes to the development and progress of the disease.

The principal cause of chronic bronchitis is prolonged irritation of the bronchial tube linings. Smoking, air pollution and recurrent infections are the main irritants for chronic bronchitis, as well as for emphysema. The public needs to be informed about the potential seriousness of persistent or recurrent coughs and shortness of breath and about ways to protect against progression of this disease.

- The program goal is to modify the smoking habits of persons at risk of developing lung diseases, and to extend successful anti-smoking programs to the general population.

Opportunities and Needs. To prevent or modify smoking habits in those at greatest risk, it is necessary first to identify persons likely to develop chronic obstructive pulmonary disease, especially those who have predisposing genetic characteristics.

We also need to prevent or modify smoking in persons who live or work in environments with unusually high concentration of air pollutants, coal dust, or other environmental agents implicated in the development of lung diseases.

Sophisticated motivation approaches must be developed to modify the smoking habits of persons at risk and, in general, large population groups. Those who have not yet acquired the habit should be discouraged from doing so through effective educational programs.

Actions. To meet these needs, the Institute will:

1. **Develop a program, in collaboration with experts from other federal agencies, to modify effectively the habits of smokers.**

2. **Develop an educational program to reach the lay public and alert it to the dangers of smoking in relation to chronic obstructive pulmonary diseases and environmental lung diseases, and urge smokers in populations at special risk to participate in programs to modify their smoking habits.**

Schedule. Behavioral and educational programs will be initiated in FY 75 to continue for five years.

PEDIATRIC PULMONARY DISEASES

Program Goals. About 40,000 babies are born each year with hyaline membrane disease. More than half of these will die unless given prompt treatment.

- Until hyaline membrane disease can be prevented the primary goal will be to initiate prompt diagnosis and therapy.

Opportunities and Needs. The opportunities and needs have been discussed above in the Research Programs section in Pediatric Pulmonary Diseases.

Action. The Institute will:

1. **Develop education programs, addressed to pulmonary and community physicians, to provide presently available information about treatment of hyaline membrane disease. This will be done through demonstration projects and workshops for physicians.**

Schedule. These education programs will be phased-in subsequent to the steadily increasing activities in therapy described under the Research Programs section in Pediatric Pulmonary Diseases. They will thus be able

to capitalize on information accruing from other new actions.

FIBROTIC AND IMMUNOLOGIC LUNG DISEASES

Program Goals. Diseases that are induced by external agents can be prevented or treated by removal of the offending substances or suppression of their effects.

- A primary program goal is to disseminate information about the causes of fibrotic and immunologic lung diseases and how to avoid them.

Opportunities and Needs. Wide dissemination of available knowledge about external agents implicated in the development of immunologic and fibrotic lung diseases should be provided to the lay public as well as to physicians. This is essential to prevention of these diseases, and is part of a more general recommendation of the Panel Chairmen to disseminate information concerning diagnosis and treatment of lung diseases.

Action. The Institute will:

1. **Develop a program of education of physicians and the lay public with regard to environmental agents implicated in pulmonary fibrosis and immunologic lung diseases. This will be accomplished through workshops for physicians, literature for the public and control programs addressed to avoidance of etiologic agents in the community.**

Schedule. The program in education regarding fibrotic and immunologic lung diseases will increase incrementally between FY 74 and FY 75.

RESPIRATORY FAILURE

Program Goals. Considerable progress has been made in the development of therapy, but unless treatment is initiated promptly by experienced personnel, respiratory failure will lead to death in more than half of those affected.

- The first goal of the program in this area is to disseminate the knowledge needed to save lives through early recognition and treatment of respiratory failure.

Opportunities and Needs. Prompt recognition of symptoms and signs of respiratory failure is essential to the early initiation of treatment. Available knowledge about detection and treatment should be widely disseminated to community physicians and allied health personnel, as well as to pulmonary physicians.

Action. The Institute will:

1. **Initiate demonstration projects in which available information will be widely disseminated to educate pulmonary and community physicians and allied health personnel in what is known about respiratory failure.**

Schedule. The major new activity will be in demonstration programs. Educational activity will undergo a delayed increase, capitalizing on new information accruing from treatment studies.

BLOOD DISEASES AND BLOOD RESOURCES

Major control programs in the blood diseases and blood resources area are concerned with sickle cell anemia and Cooley's anemia. Other efforts include programs in hemophilia and certain aspects of blood resources.

SICKLE CELL ANEMIA AND COOLEY'S ANEMIA

Program Goals. Despite the fact that much is known about sickle cell disease and Cooley's anemia, the general public, including actual and potential victims, have a poor understanding of these disorders and their ramifications. The NHLI is developing a program to expand community education to increase public awareness regarding these diseases and to educate these individuals.

- The goals of the control program are to educate the public about sickle cell disease and Cooley's anemia and to demonstrate techniques for appropriate screening and counseling.

Opportunities and Needs. We need to determine the prevalence and distribution of sickle cell disease and Cooley's anemia in this country, particularly the prevalence of carriers of the trait; provide accurate and up-to-date information on these diseases; initiate and expand appropriate community education, screening, and counseling programs; educate the medical and

allied health professions about the problems of these diseases; identify and provide guidance for the management of the resulting psychological, sociological and economic problems; and assist individuals with these disorders to attain their maximum potential in life.

Actions. To meet these needs, the Institute will:

1. **Develop, in collaboration with other federal agencies, programs to provide accurate information on sickle cell disease and Cooley's anemia; education for the general public, population groups at risk, health professionals, allied health professionals, educators, employers, and insurers of individuals who have these disorders; methods to best counsel affected individuals; and proper rehabilitation approaches when applicable.**

2. **Evaluate clinical approaches for the treatment of these disorders and ensure that the ones that work are incorporated into the health delivery system.**

Schedule. Screening and Education Clinics for sickle cell disease will continue to be heavily supported in FY 74 and 75. Information and education programs on both sickle cell disease and Cooley's anemia will be supported in FY 74 with a gradual reduction of activity from FY 76 to FY 79.

HEMOPHILIA

Program Goals. Public awareness is fundamental to prevention of hemophilia.

- The goal of the prevention effort in hemophilia is to educate the public so that hemophilia carriers and patients may make informed decisions regarding their own lives.

Opportunities and Needs. Genetic counseling is not working. Unless it can be made to work or unless means of prevention are discovered, the hemophilic population will grow. The Blood Diseases Panel, the Panel Chairmen, and the National Heart and Lung Advisory Council all urge that a strong and positive program of genetic research and counseling be established.

Action. The Institute will:

1. **Develop information, education and genetic counseling services aimed at better treatment and prevention.**

Schedule. Information, education and genetic counseling in hemophilia will receive increased support in FY 76 and FY 77, and we anticipate major program activity in genetic counseling by FY 79.

BLOOD RESOURCES

Program Goals. Special efforts are needed to encourage more effective and economic utilization of the nation's blood resources. A continuing program must be carried out for professional and public information and education about blood resources and the use of effective blood management systems. This is especially true of blood component therapy.

- The goal of this program is to effect, from dissemination of information and education, improved management of the nation's blood resources.

Opportunities and Needs. We need to develop ways to educate the physician regarding optimal use of blood components in order to moderate his demands on the nation's blood resources.

Action. The Institute will:

1. **Support continuous physician education regarding optimal use of blood components.**

Schedule. The Institute's progress in educational programs in blood therapy will be increased gradually over the next five years.

OVERALL ACTIONS AND SCHEDULE

There are certain action programs and schedules which are applicable in general to all the disease problem areas and which the Institute will initiate.

Actions. In planning for a more effective National Program in consumer and professional information and education, the Institute will:

1. **Develop information programs for each of the categorical program areas of the Institute.**

2. **Develop better mechanisms, using all media of communication, to disseminate information on heart, blood vessel, lung and blood diseases and blood resources.**

3. Establish improved means for direct communication with the public.

4. Expand programs to aid health professionals in improving the public's understanding and application of new health knowledge and concepts.

5. Establish improved means for communication with the scientific community and the medical profession.

The NHLI information and education programs will be developed with the following populations in mind:

- Young people
- Adult population in general
- Individuals who have heart and blood vessel, lung or blood diseases which fall within the mission of the NHLI
- Individuals who may be especially susceptible to heart, blood vessel or lung diseases
- Health professionals.

The enhanced public education program will stress certain general concepts regarding these disease problems:

- Heart and blood vessel diseases include many different diseases of the heart and circulation.
- Some heart and lung diseases are preventable; for example, rheumatic heart disease following acute communicable streptococcal infection.
- Early prevention, starting in youth, is important.
- Virtually all types of heart and blood vessel, lung and blood diseases can be handled best if diagnosed early and treated properly.
- More patients with heart and blood vessel, lung and blood diseases can be significantly improved by proper treatment, management and rehabilitation.
- Heart, blood vessel, lung and blood diseases do not necessarily prevent one from living comfortably and earning a living, providing the type of work is selected according to the limitations of the individuals.

Schedule. The Institute's current programs in Prevention, Control and Education are modest. The NHLI proposes to place considerable emphasis on information and education programs during the next five years.

V. THE NHLI RESOURCE ALLOCATION PLAN

In developing the NHLI Program Plan, the Institute has given consideration to the resources—fiscal, manpower and facilities—that will be needed to achieve the overall goals of advancing the attack on heart, blood vessel, lung and blood diseases, and the specific program goals. The Legislation, Section 413 (b) (1), directs the National Heart and Lung Institute to set out, as part of its plan, "the Institute's staff requirements to carry out the Program and recommendations for appropriations for the Program." From the approximately 2000 potential projects proposed and reviewed by the Task Groups, the Panels, the Panel Chairmen and the National Heart and Lung Advisory Council, the Institute has selected the most urgent and opportune recommendations for implementation during the first five years of the National Program. Prior to setting forth its recommendations, the Institute has also reviewed its current program commitments, activities, and plans, information on programs of other federal agencies and nonfederal organizations, as well as the resource allocations projected by the Panel Chairmen and the National Heart and Lung Advisory Council. Our priority actions have been set forth in the previous section and the resources needed to fulfill these NHLI-supported actions are set forth here. Contributions by non-NHLI supported activities are not included in these resource projections.

FISCAL SUMMARY AND PROJECTIONS

The projected fiscal allocation scheme takes into account the legislative requirement that not less than 15 percent of the fiscal resources shall be applied toward solving the problems of diseases of the lung, and that not less than 15 percent of the fiscal resources, likewise, shall be applied toward the problems of blood diseases. The projected budget allocations for Fiscal Years 1974 to 1979 are shown in Table 6. A six-year projection is given so that the planning process will become in phase with the overall department planning and budgeting cycle. These allocations are organized according to the disease categories discussed in earlier sections of this Summary. The Table sets forth fiscal projections for Extramural Research Programs in Heart and Blood Vessel Diseases, in Lung Diseases, and in Blood Diseases and Blood Resources. Proposed allocations are also shown for each of the major problem areas within the disease categories considered in the NHLI Program Plan. Funding required to implement new authorizations provided by the Act are also projected and include National Research and Demonstration Centers; prevention, control and education programs; and, beginning in FY 75, construction of facilities. Support for current manpower programs is also included. Finally, a projection is provided for the Intramural Research Program, with an increase of approximately $1.6 million for FY 74 for new initiatives, primarily in the lung and blood diseases area.

The fiscal requirements for FY 74 for the proposed National Program total $311 million for FY 74, an increase of $46 million over the previously proposed budget. These requirements increase incrementally each year except for FY 78 when resources for construction will not be required. In FY 79, the total fiscal resources required for the Program will be $429 million.

Table 6

PROJECTED RESOURCE ALLOCATIONS FOR THE NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM, FY 74 - FY 79 (DOLLARS IN MILLIONS)

Program Activities	Fiscal Years					
	1974	1975	1976	1977	1978	1979
Extramural Research Programs						
Heart and Blood Vessel Diseases						
Arteriosclerosis	$ 51.75	$ 53.55	$ 55.95	$ 56.50	$ 63.20	$ 61.65
Hypertension	20.99	24.95	28.10	29.30	34.70	34.80
Cerebrovascular Disease	2.16	2.45	2.50	2.81	3.60	3.70
Coronary Heart Disease	41.25	42.25	47.35	52.00	53.00	47.50
Peripheral Vascular Diseases	3.50	4.00	4.25	3.75	4.00	4.25
Arrhythmias	10.35	12.20	14.00	13.00	13.00	12.00
Heart Failure and Shock*	32.00	37.65	39.20	38.89	38.20	59.70
Congenital and Rheumatic Heart Diseases	9.50	10.25	10.85	11.45	12.50	12.50
Cardiomyopathy and Infections of the Heart	4.50	5.70	7.00	7.70	8.00	8.00
Subtotal, Heart and Blood vessel Diseases	176.00	193.00	209.20	215.40	230.20	244.10
Lung Diseases						
Structure and Function of the Lung	5.00	5.00	5.20	5.20	5.70	7.40
Pediatric Pulmonary Diseases	5.53	6.50	6.80	7.20	7.70	8.20
Emphysema and Chronic Bronchitis	12.57	13.50	13.80	13.50	13.40	13.30
Fibrotic and Immunologic Lung Diseases	7.50	8.80	9.90	11.00	11.80	13.30
Respiratory Failure	9.20	10.80	11.50	12.90	14.40	13.80
Subtotal, Lung Diseases	39.80	44.60	47.20	49.80	53.00	56.00
Blood Diseases and Blood Resources						
Bleeding and Clotting Disorders**	21.24	22.33	22.64	24.08	23.18	23.93
Sickle Cell Disease and Related Disorders of the Red Blood Cell	16.60	16.67	18.05	18.77	20.44	20.32
Blood Resources	10.26	12.30	14.81	14.95	17.18	19.65
Subtotal, Blood Diseases and Blood Resources	48.10	51.30	55.50	57.80	60.80	63.90
National Research and Demonstration Centers	5.00	15.00	25.00	30.00	30.00	30.00
Prevention, Control and Education Programs	3.00	8.00	10.00	12.00	10.00	8.00
Construction	--	20.00	30.00	20.00	--	--
Manpower	17.10	10.10	3.10	2.00	1.00	1.00
Intramural Research Program	22.00	23.00	25.00	26.00	26.00	26.00
Total	$311.00	$365.00	$405.00	$413.00	$411.00	$429.00

*Includes circulatory assist and artificial heart research and development
**Includes biomaterials research and development

MECHANISMS OF SUPPORT

The Intramural Research Program is an in-house activity of basic and clinical research on heart and blood vessel, lung and blood diseases. All other program activities are supported extramurally, either by grants or contracts. These mechanisms of support are used by the NHLI to fulfill statutory purposes, by providing funding to organizations external to the Institute. The current allocation of funds to these two mechanisms and to other major activities of the Institute is shown in Table 7.

Table 7

NHLI RESOURCE ALLOCATION BY MAJOR ACTIVITY, FY 1973

Activity	Percent
Research Grants	54.8
Training Grants and Fellowships	8.9
Research Contracts	24.0
Intramural Research	7.6
Research Management and Program Services	4.7
Total	100.0

In implementing the plan for a National Heart, Blood Vessel, Lung and Blood Program, the NHLI plans to provide the widest possible range of mechanisms of support for programs in research, prevention, demonstration, and education. This will involve a spectrum of mechanisms ranging from highly structured targeted programs at one end to less structured, investigator-initiated programs at the other end. Whatever the mechanism, it is necessary to provide direction to the activity, as well as to allow for creativity and discovery.

As noted in the Report of the National Heart and Lung Advisory Council, "Some investigators do their best work alone, others do best when working in small groups; still others are most productive when they have the stimulus that comes from frequent exchange of ideas in a large interdisciplinary center." Furthermore, specific, well-defined activities needed to accomplish particular coordinated or multidisciplinary objectives in the National Program will be planned for and directed by the Institute. Other program activities, such as the elucidation of more fundamental knowledge in a particular disease or problem area will be developed by encouraging individual scientists to initiate new approaches and investigations.

The most appropriate fiscal mechanism must be selected for each program activity. The research grant is the preferred mechanism of support for investigator-initiated and directed research, whereas the research contract is preferred if the project is initiated by the Institute. The research grant is proposed by the scientist to the National Institutes of Health. Almost all contract proposals are received in response to a Request for Proposal (RFP) announcement by the Institute, setting forth the specific objectives of the intended project. Grant and contract proposals are evaluated by similar mechanisms. Research grants are first reviewed by technical panels of experts, or study sections, for scientific merit, and secondarily by the National Heart and Lung Advisory Council for program relevance. Research contracts are also reviewed by nongovernment panels of experts for scientific merit and responsiveness to predetermined program objectives and secondarily by program officials and the executive staff of the Institute. After review and evaluation of the initial proposals, grants or contracts are awarded and activity is initiated. Thereafter, subsequent periodic scientific review and evaluation and continued program relevance determine whether a given project is continued. The NHLI believes these mechanisms of support are fundamental to the Institute's mission.

NATIONAL RESEARCH AND DEMONSTRATION CENTERS

Section 415 of the Act authorizes up to 15 National Research and Demonstration Centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods for heart, blood vessel, and blood diseases, and 15 centers for similar purposes for chronic lung diseases. The activities of any particular center may be limited to one disease area or encompass them all.

The reports of the Task Force on Arteriosclerosis in 1971, the Panel Chairmen, and the National Heart and Lung Advisory Council all recommend interdisciplinary, multicategorical centers as a means of furthering the goals of the National Program. There are many advantages to such organizational units: The "critical mass" of scientists representing many disciplines working in a coordinated way toward the solution of common problems can speed the solution of the problems; the interaction between fundamental scientists and clinicians can assure the rapid translation of the results of research into patient care; and, problems encountered in patients can be taken back to the laboratory for further study. The National Research and Demonstration Centers can also be effective in training the different types of manpower needed for a total national effort in heart and blood vessel, lung and blood diseases. The application of new techniques and treatments can also be demonstrated by the center through the health care system as it actually exists in the community.

Certain disadvantages of these centers have also been considered: They may negatively affect program activities of existing biomedical institutions, particularly by attracting trained manpower needed by these institutions; too many centers, established in haste, could effect a redistribution of trained persons from present widely dispersed programs throughout the nation into a few center locations; the complex organization of a center—multidepartmental, multidisciplinary, and involving community resources—may create administrative difficulties for the sponsoring organization and for the NHLI; and, possible self-perpetuation, once a center is established, is a potential danger.

Having considered all these advantages and disadvantages and the recommendations of the advisory groups mentioned above, the NHLI concludes that the advantages outweigh the disadvantages and that the goals of the National Program will be furthered by the establishment of National Research and Demonstration Centers. At the present time, we envisage the centers authorized in Section 415 as comprehensive in scope—encompassing a broad spectrum of activities from fundamental research, through clinical investigation, to demonstration of applicability of research results in the health care system of the community. It is not intended that the centers become involved in health care delivery beyond programs initiated for demonstration purposes. Resources are projected for the establishment of approximately five centers in FY 74 and an additional five in FY 75. The initial level of support required from the NHLI is projected at approximately $1 million for each center, with fiscal increases as each center develops to approximately $3 million in the third year.

CONSTRUCTION

The National Heart and Lung Advisory Council notes in its report the need for more facilities in order to accommodate the broad scope of the National Program. The level of support authorized as a ceiling for each National Research and Demonstration Center is $5 million, which is exclusive of construction. If such centers are established *de novo* as free-standing, independent units, it is probable that construction of the entire facility will have to be provided. What is far more likely, however, is that centers will be established as part of an existing medical complex which will make a considerable commitment to the center in facilities and resources. Even under these circumstances, limited construction of additional facilities will be necessary. The Institute estimates that the net space requirements for each unit will approximate 80 to 100 thousand square feet and that, on the average, approximately 60 percent of the space will have to be newly constructed. Accordingly, funds are projected for 160 thousand square feet in FY 75, 240 thousand in FY 76 and 160 thousand square feet in FY 77.

Because the planning and execution of a construction project often takes longer than anticipated, it is requested that funds appropriated for construction purposes remain available to the Institute for use for this purpose during the year subsequent to the one in which such funds are appropriated.

MANPOWER DEVELOPMENT

Supply of skilled manpower is an essential element in a national effort designed to advance the attack upon heart, blood vessel, lung and blood diseases. An adequate long-range plan in an expanding program directed against these diseases will require an expanding manpower pool to conduct needed research and to replace skilled manpower lost through attrition. As noted by the Panel Chairmen and the National Heart and Lung Advisory Council, a critical need now for long-term success of the National Program is recruitment and training of talented young scientists who can replace retiring investigators and who can be encouraged to explore new and opening areas of research.

Implementation of the National Program necessitates continual assessment of available manpower—both in numbers and disciplines. The number of well-trained scientists, clinicians, and allied health professionals—in many different fields—will have to be balanced with the National Program activities. If the needs of the Program are not met through available mechanisms, we will recommend appropriate changes. The Institute proposes to monitor the progress of the National Program with particular reference to the availability of manpower needed to achieve its objectives. As the Programs moves forward, we will develop specific recommendations as appropriate in the annual progress reports.

NHLI STAFF ALLOCATION PLAN

The Act requires that the plan include recommendations regarding NHLI staffing needs for implementation of the National Program. The Institute has assumed a number of new activities in accordance with the Legislation, such as annual updating of the five-year plan for the National Program, annual reports by the Director and the Council, management of the Interagency Technical Committee, initiation of education and control programs, and development of National Research and Demonstration Centers. Implementation of the National Program designed to carry out these new activities will require the Institute staff to assume greater responsibilities for analysis and evaluation of programs, identification of neglected gaps and overlaps in program content, initiation of new programs, and coordination of the national effort.

All of the scientific program divisions of the Institute will be mounting new programs that will require increased manpower for effective coordination and evalution. For example, Specialized Centers of Research are planned in several areas, including centers for heart and lung diseases of children; work in the area of lung diseases, now in its early stages, is expanding substantially in several directions; the new National Research and Demonstration Centers will require special staff; the development of noninvasive techniques for diagnosis and monitoring, stressed by each of the advisory Panels and by the National Heart and Lung Advisory Council, will require staff members with knowledge of special areas; the Division of Extramural Affairs will need additional staff with expertise in reviewing applications and proposals in areas entirely new to the Institute, such as the National Research and Demonstration Centers and the control programs; and the Intramural Research Program plans to expand investigations in areas of lung and blood diseases.

The demands of new initiatives and the expansion of current programs will require additional staff in numbers and require expertise that is not now available within the Institute. Therefore, the Institute proposes to fill many of the new positions with professional scientists at middle to upper appointment levels to handle the additional responsibilities called for by the National Program.

The current authorized positions within the Institute number 626. It is projected that this number should be increased to 764 in FY 74 and further increased to approximately 810 in FY 76. After that, we anticipate that the level will remain essentially unchanged.

APPENDIX A
NATIONAL HEART, BLOOD VESSEL, LUNG, AND BLOOD ACT OF 1972

This Appendix presents the Legislation (Public Law 92-423), enacted on September 19, 1972, which set into motion an intensive six-month planning effort directed by the National Heart and Lung Institute to formulate a National Program to combat heart and blood vessel, lung and blood diseases, and blood resource problems.

Public Law 92-423
92nd Congress, S. 3323
September 19, 1972

An Act

To amend the Public Health Service Act to enlarge the authority of the National Heart and Lung Institute in order to advance the national attack against diseases of the heart and blood vessels, the lungs, and blood, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled.

National Heart, Blood Vessel, Lung, and Blood Act of 1972.

SHORT TITLE

SECTION 1. This Act may be cited as the "National Heart, Blood Vessel, Lung, and Blood Act of 1972".

FINDINGS AND DECLARATION OF PURPOSE

SEC. 2. (a) Congress finds and declares that—

(1) diseases of the heart and blood vessels collectively cause more than half of all the deaths each year in the United States and the combined effect of the disabilities and deaths from such diseases is having a major social and economic impact on the Nation;

(2) elimination of heart and blood vessel diseases as significant causes of disability and death could increase the average American's life expectancy by about eleven years and could provide for annual savings to the economy in lost wages, productivity, and costs of medical care of more than $30,000,000,000 per year;

(3) chronic lung diseases have been gaining steadily in recent years as important causes of disability and death, with emphysema alone being the fastest rising cause of death in the United States;

(4) chronic respiratory diseases affect an estimated ten million Americans, emphysema an estimated one million, chronic bronchitis an estimated four million, and asthma an estimated five million;

(5) thrombosis (the formation of blood clots in the vessels) may cause, directly or in combination with other problems, many deaths and disabilities from heart disease and stroke which can now be prevented; 86 STAT. 679

(6) blood and blood products are essential human resources 86 STAT. 680 whose value in saving life and promoting health cannot be assessed in terms of dollars;

(7) the provision of prompt and effective emergency medical services utilizing to the fullest extent possible advances in transportation and communications and other electronic systems and specially trained professional and paraprofessional health care personnel can reduce substantially the number of fatalities and severe disabilities due to critical illnesses in connection with heart, blood vessel, lung, and blood diseases; and

(8) the greatest potential for advancement against heart, blood vessel, lung, and blood diseases lies in the National Heart and Lung Institute, but advancement against such diseases depends not only on the research programs of that Institute but also on the research programs of other research institutes of the National Institutes of Health.

(b) It is the purpose of this Act to enlarge the authority of the National Heart and Lung Institute in order to advance the national attack upon heart, blood vessel, lung, and blood diseases.

83-749 O (260)

HEART, BLOOD VESSEL, LUNG, AND BLOOD DISEASE PROGRAMS

62 Stat. 464. 42 USC 287-287c.

SEC. 3. Part B of title IV of the Public Health Service Act is amended (1) by redesignating section 413 as section 419A. (2) by redesignating section 414 as section 418, and (3) by adding after section 412 the following new sections:

"NATIONAL HEART, BLOOD VESSEL, LUNG, AND BLOOD DISEASE PROGRAM

"SEC. 413. (a) The Director of the Institute, with the advice of the Council, shall develop a plan for a National Heart, Blood Vessel, Lung, and Blood Disease Program (hereafter in this part referred to as the 'Program') to expand, intensify, and coordinate the activities of the Institute respecting heart, blood vessel, lung, and blood diseases (including its activities under section 412) and shall carry out the Program in accordance with such plan. The Program shall be coordinated with the other research institutes of the National Institutes of Health to the extent that they have responsibilities respecting such diseases and shall provide for—

NIH, coordination provisions.

"(1) investigation into the epidemiology, etiology, and prevention of all forms and aspects of heart, blood vessel, lung, and blood diseases, including investigations into the social, environmental, behavioral, nutritional, biological, and genetic determinants and influences involved in the epidemiology, etiology, and prevention of such diseases;

"(2) studies and research into the basic biological processes and mechanisms involved in the underlying normal and abnormal heart, blood vessel, lung, and blood phenomena;

"(3) research into the development, trial, and evaluation of techniques, drugs, and devices (including computers) used in, and approaches to, the diagnosis, treatment (including emergency medical service), and prevention of heart, blood vessel, lung, and blood diseases and the rehabilitation of patients suffering from such diseases;

86 STAT. 680

86 STAT. 681

"(4) establishment of programs that will focus and apply scientific and technological efforts involving biological, physical, and engineering sciences to all facets of heart, blood vessel, lung, and blood diseases with emphasis on refinement, development, and evaluation of technological devices that will assist, replace, or monitor vital organs and improve instrumentation for detection, diagnosis, and treatment of those diseases;

"(5) establishment of programs for the conduct and direction of field studies, large-scale testing and evaluation, and demonstration of preventive, diagnostic, therapeutic, and rehabilitative approaches to, and emergency medical services for, such diseases;

"(6) studies and research into blood diseases and blood, and into the use of blood for clinical purposes and all aspects of the management of its resources in this country, including the collection, preservation, fractionalization, and distribution of it and its products;

"(7) the education and training of scientists, clinicians, and educators, in fields and specialties (including computer sciences) requisite to the conduct of programs respecting heart, blood vessel, lung, and blood diseases;

"(8) public and professional education relating to all aspects of such diseases and the use of blood and blood products and the management of blood resources:

"(9) establishment of programs for study and research into heart, blood vessel, lung, and blood diseases of children (including cystic fibrosis, hyaline membrane, and hemolytic and hemophilic

diseases) and for the development and demonstration of diagnostic, treatment, and preventive approaches to these diseases; and

"(10) establishment of programs for study, research, development, demonstrations and evaluation of emergency medical services for people who become critically ill in connection with heart, blood vessel, lung, or blood diseases, which programs shall include programs for (A) the training of paraprofessionals in (i) emergency treatment procedures, and (ii) utilization and operation of emergency medical equipment, (B) the development and operation of (i) mobile critical care units (including helicopters and other airborne units where appropriate), (ii) radio, telecommunications, and other means of communications, and (iii) electronic monitoring systems, and (C) the coordination with other community services and agencies in the joint use of all forms of emergency vehicles, communications systems, and other appropriate services.

The Program shall give special emphasis to the continued development in the Institute of programs relating to atherosclerosis, hypertension, thrombosis, and congenital abnormalities of the blood vessels as causes of stroke, and to effective coordination of such programs with related stroke programs in the National Institute of Neurological Diseases and Stroke. National Institute of Neurological Diseases and Stroke, coordination.

"(b)(1) The plan required by subsection (a) of this section shall (A) be developed within one hundred and eighty days after the effective date of this section, (B) be transmitted to the Congress, and (C) set out the Institute's staff requirements to carry out the Program and recommendations for appropriations for the Program. Plan development; transmittal to Congress. 86 STAT. 681 86 STAT. 682

"(2) The Director of the Institute shall, as soon as practicable after the end of each calendar year, prepare in consultation with the Council and submit to the President for transmittal to the Congress a report on the activities, progress, and accomplishments under the Program during the preceding calendar year and a plan for the Program during the next five years. Report to President, transmittal to Congress.

"(c) In carrying out the Program, the Director of the Institute, under policies established by the Director of the National Institutes of Health and after consultation with the Council and without regard to any other provision of this Act, may— Director, functions.

"(1) if authorized by the Council, obtain (in accordance with section 3109 of title 5, United States Code, but without regard to the limitation in such section on the number of days or the period of such service) the services of not more than fifty experts or consultants who have scientific or professional qualifications; 80 Stat. 416.

"(2) acquire, construct, improve, repair, operate, and maintain heart, blood vessel, lung, and blood disease laboratory, research, training, and other necessary facilities and equipment, and related accommodations as may be necessary, and such other real or personal property (including patents) as the Director deems necessary; and acquire, without regard to the Act of March 3, 1877 (40 U.S.C. 34), by lease or otherwise, through the Administrator of General Services, buildings or parts of buildings in the District of Columbia or communities located adjacent to the District of Columbia for the use of the Institute for a period not to exceed ten years; and 19 Stat. 370.

"(3) enter into such contracts, leases, cooperative agreements, or other transactions, without regard to sections 3648 and 3709 of the Revised Statutes of the United States (31 U.S.C. 529, 41 U.S.C. 5), as may be necessary in the conduct of his functions, with any public agency, or with any person, firm, association, corporation, or educational institution.

Assistant Director for Health Information Programs. Cardiovascular and pulmonary diseases, information.

"(d) There shall be in the Institute an Assistant Director for Health Information Programs who shall be appointed by the Director of the Institute. The Director of the Institute, acting through the Assistant Director for Health Information Programs, shall conduct a program to provide the public and the health professions with health information with regard to cardiovascular and pulmonary diseases. In the conduct of such program, special emphasis shall be placed upon dissemination of information regarding diet, exercise, stress, hypertension, cigarette smoking, weight control, and other factors affecting the prevention of arteriosclerosis and other cardiovascular diseases and of pulmonary diseases.

"HEART, BLOOD VESSEL, LUNG, AND BLOOD DISEASE PREVENTION AND CONTROL PROGRAMS

"SEC. 414. (a) The Director of the Institute, under policies established by the Director of the National Institutes of Health and after consultation with the Council, shall establish programs as necessary for cooperation with other Federal Health agencies, State, local, and regional public health agencies, and nonprofit private health agencies in the diagnosis, prevention, and treatment (including the provision of emergency medical services) of heart, blood vessel, lung, and blood diseases, appropriately emphasizing the prevention, diagnosis, and treatment of such diseases of children.

86 STAT. 682
86 STAT. 683

Appropriations.

"(b) There is authorized to be appropriated to carry out this section $25,000,000 for the fiscal year ending June 30, 1973, $35,000,000 for the fiscal year ending June 30, 1974, and $45,000,000 for the fiscal year ending June 30, 1975.

"NATIONAL RESEARCH AND DEMONSTRATION CENTERS FOR HEART, BLOOD VESSEL, LUNG, AND BLOOD DISEASES

"SEC. 415. (a)(1) The Director of the Institute may provide for the development of—

"(A) fifteen new centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods (including methods of providing emergency medical services) for heart, blood vessel, and blood diseases; and

"(B) fifteen new centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods (including methods of providing emergency medical services) for chronic lung diseases (including bronchitis, emphysema, asthma, cystic fibrosis, and other lung diseases of children).

"(2) The centers developed under paragraph (1)(A) shall, in addition to being utilized for research, training, and demonstrations, be utilized for the following prevention programs for cardiovascular diseases:

"(A) Programs to develop improved methods of detecting individuals with a high risk of developing cardiovascular disease.

"(B) Programs to develop improved methods of intervention against those factors which cause individuals to have a high risk of developing such disease.

"(C) Programs to develop health professions and allied health professions personnel highly skilled in the prevention of such disease.

"(D) Programs to develop improved methods of providing emergency medical services for persons with such disease.

"(3) Centers developed under this subsection may be supported under subsection (b) or under any other applicable provision of law. The research, training, and demonstration activities carried out through any such center may relate to any one or more of the diseases referred to in paragraph (1) of this subsection.

"(b) The Director of the Institute, under policies established by the Director of the National Institutes of Health and after consultation with the Council, may enter into cooperative agreements with public or nonprofit private agencies or institutions to pay all or part of the cost of planning, establishing, or strengthening, and providing basic operating support for, existing or new centers (including centers established under subsection (a)) for basic or clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods for heart, blood vessel, lung, or blood diseases. Funds paid to centers under cooperative agreements under this subsection may be used for— Public or nonprofit agencies, cooperative agreements. Use of funds.

"(1) construction, notwithstanding section 405, 58 Stat. 708.

"(2) staffing and other basic operating costs, including such patient care costs as are required for research, 42 USC 285. 86 STAT. 683

"(3) training, including training for allied health professions personnel, and 86 STAT. 684

"(4) demonstration purposes.

The aggregate of payments (other than payments for construction) made to any center under such an agreement may not exceed $5,000,000 in any year. Support of a center under this subsection may be for a period of not to exceed five years and may be extended by the Director of the Institute for additional periods of not more than five years each, after review of the operations of such center by an appropriate scientific review group established by the Director. As used in this section, the term 'construction' does not include the acquisition of land. Limitations. "Construction."

"INTERAGENCY TECHNICAL COMMITTEE

"SEC. 416. (a) The Secretary shall establish an Interagency Technical Committee on Heart, Blood Vessel, Lung and Blood Diseases and Blood Resources which shall be responsible for coordinating those aspects of all Federal health programs and activities relating to heart, blood vessel, lung, and blood diseases and to blood resources to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities. Establishment.

"(b) The Director of the Institute shall serve as Chairman of the Committee and the Committee shall include representation from all Federal departments and agencies whose programs involve health functions or responsibilities as determined by the Secretary.

"NATIONAL HEART AND LUNG ADVISORY COUNCIL

"SEC. 417. (a) There is established in the Institute a National Heart and Lung Advisory Council to be composed of twenty-three members as follows: Establishment; membership.

"(1) The Secretary, the Director of the National Institutes of Health, the Director of the Office of Science and Technology, and the chief medical officer of the Veterans' Administration (or their designees), and a medical officer designated by the Secretary of Defense, shall be ex officio members of the Council.

"(2) Eighteen members appointed by the Secretary.

Eleven of the appointed members shall be selected from among the leading medical or scientific authorities who are skilled in the sciences

relating to diseases of the heart, blood vessels, lungs, and blood; two of the appointed members shall be selected from persons enrolled in residency programs providing training in heart, blood vessel, lung, or blood diseases; and five of the appointed members shall be selected from members of the general public who are leaders in the fields of fundamental or medical sciences or in public affairs.

Terms.

"(b)(1) Each appointed member of the Council shall be appointed for a term of four years, except that—

"(A) any member appointed to fill a vacancy occurring prior to the expiration of the term for which his predecessor was appointed shall be appointed for the remainder of such term; and

86 STAT. 684

86 STAT. 685

"(B) of the members first appointed after the effective date of this section, five shall be appointed for a term of four years, five shall be appointed for a term of three years, five shall be appointed for a term of two years, and three shall be appointed for a term of one year, as designated by the Secretary at the time of appointment.

Extension.

Appointed members may serve after the expiration of their terms until their successors have taken office.

"(2) A vacancy in the Council shall not affect its activities, and twelve members of the Council shall constitute a quorum.

National Advisory Heart Council, replacement provisions.

64 Stat. 446.

42 USC 218.

"(3) The Council shall supersede the existing National Advisory Heart Council appointed under section 217, and the appointed members of the National Advisory Heart Council serving on the effective date of this section shall serve as additional members of the National Heart and Lung Advisory Council for the duration of their terms then existing, or for such shorter time as the Secretary may prescribe.

"(4) Members of the Council who are not officers or employees of the United States shall receive for each day they are engaged in the performance of the functions of the Council compensation at rates not to exceed the daily equivalent of the annual rate in effect for grade GS-18 of the General Schedule, including traveltime; and all members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703 of title 5, United States Code, for persons in the Government service employed intermittently.

5 USC 5332 note.

80 Stat. 499; 83 Stat. 190.

"(c) The Secretary (or his designee) shall be the Chairman of the Council.

Executive Secretary.

"(d) The Director of the Institute shall (1) designate a member of the staff of the Institute to act as Executive Secretary of the Council, and (2) make available to the Council such staff, information, and other assistance as it may require to carry out its functions.

"(e) The Council shall meet at the call of the Chairman, but not less often than four times a year."

AUTHORIZATION OF APPROPRIATIONS FOR PART B OF TITLE IV OF THE PUBLIC HEALTH SERVICE ACT

Ante, p. 680.

SEC. 4. Part B of title IV of the Public Health Service Act is amended by adding at the end thereof the following new section:

"AUTHORIZATION OF APPROPRIATIONS

Ante, p. 682.

"SEC. 419B. For the purpose of carrying out this part (other than section 414), there is authorized to be appropriated $375,000,000 for the fiscal year ending June 30, 1973, $425,000,000 for the fiscal year ending June 30, 1974, and $475,000,000 for the fiscal year ending June 30, 1975. Of the sums appropriated under this section for any fiscal year, not less than 15 per centum of such sums shall be reserved

for programs under this part respecting diseases of the lung and not less than 15 per centum of such sums shall be reserved for programs under this part for programs respecting diseases of the blood."

AUTHORITY OF THE DIRECTOR OF THE NATIONAL HEART AND LUNG INSTITUTE TO APPROVE GRANTS

SEC. 5. Section 419A of the Public Health Service Act (as so redesignated by section 3 of this Act) is amended—

(1) by striking out "grants-in-aid" in subsection (a) and inserting in lieu thereof "except as provided in subsection (c), grants-in-aid"; and

(2) by adding after subsection (b) the following new subsection:

"(c) Under procedures approved by the Director of the National Institutes of Health, the Director of the National Heart and Lung Institute may approve grants under this Act for research and training in heart, blood vessel, lung, and blood diseases—

"(1) in amounts not to exceed $35,000 after appropriate review for scientific merit but without review and recommendation by the Council, and Limitations.

"(2) in amounts exceeding $35,000 after appropriate review for scientific merit and recommendation for approval by the Council."

CONFORMING AMENDMENTS TO PART B OF TITLE IV OF THE PUBLIC HEALTH SERVICE ACT

SEC. 6. (a) Section 411 of the Public Health Service Act is amended by striking out "National Heart Institute" and inserting in lieu thereof "National Heart and Lung Institute". 62 Stat. 465. 42 USC 287.

(b) Section 412 of such Act is amended— 42 USC 287a.

(1) by striking out "heart" each place it occurs (except in the heading) and inserting in lieu thereof "heart, blood vessel, lung, and blood";

(2) by striking out "Surgeon General" and inserting in lieu thereof "Secretary";

(3) by striking out "National Advisory Heart Council" and inserting in lieu thereof "National Heart and Lung Advisory Council";

(4) by redesignating paragraphs (a), (b), (c), (d), (e), (f), and (g) as paragraphs (1), (2), (3), (4), (5), (6), and (7), respectively; and

(5) by amending the section heading to read as follows:

"RESEARCH AND TRAINING IN DISEASES OF THE HEART, BLOOD VESSELS, LUNG, AND BLOOD"

(c) Section 418 of such Act (as so redesignated by section 3 of this Act) is amended—

(1) by inserting "(a)" immediately after "SEC. 418." and by adding at the end thereof the following new subsection:

"(b)(1) The Council shall advise and assist the Director of the Institute with respect to the Program established under section 413. The Council may hold such hearings, take such testimony, and sit and act at such times and places, as the Council deems advisable to investigate programs and activities of the Program. Ante, p. 680.

"(2) The Council shall submit a report to the President for transmittal to the Congress not later than January 31 of each year on the progress of the Program toward the accomplishment of its objectives." Report to President, transmittal to Congress.

(2) by striking out "Surgeon General" each place it occurs (except paragraph (f)) and inserting in lieu thereof "Secretary";

(3) by striking out "heart" each place it occurs and inserting in lieu thereof "heart, blood vessel, lung, and blood";

(4) by striking out "Surgeon General" in paragraph (f) and inserting in lieu thereof "Secretary, the Director of the National Institutes of Health, and the Director of the National Heart and Lung Institute"; and

(5) by redesignating paragraphs (a), (b), (c), (d), (e), and (f) as paragraphs (1), (2), (3), (4), (5), and (6), respectively.

(d) Section 419A of such Act (as so redesignated by section 3 of this Act) is amended—

(1) in subsection (a), by (A) striking out "Surgeon General" and inserting in lieu thereof "Secretary", and (B) striking out "heart" and inserting in lieu thereof "heart, blood vessel, lung, and blood"; and

(2) in subsection (b), by (A) striking out "The Surgeon General shall recommend to the Secretary acceptance of conditional gifts, pursuant to section 501," and inserting in lieu thereof "The Secretary may, in accordance with section 501, accept conditional gifts", and (B) striking out "heart" and inserting in lieu thereof "heart, blood vessel, lung, and blood".

58 Stat. 709.
42 USC 219.

(e) The heading for part B of such Act is amended to read as follows:

"PART B—NATIONAL HEART AND LUNG INSTITUTE".

CONFORMING AMENDMENTS TO OTHER PROVISIONS OF THE PUBLIC HEALTH SERVICE ACT

SEC. 7. (a) Section 217 of such Act is amended—

64 Stat. 446.
42 USC 218.

(1) by striking out "the National Advisory Heart Council," each place it occurs in subsection (a);

(2) by striking out "heart diseases," in subsection (a) and by striking out "heart," in subsection (b).

58 Stat. 692;
62 Stat. 601;
79 Stat. 448.
42 USC 241.

(b) Sections 301(d) and 301(i) of such Act are each amended by striking out "National Advisory Heart Council" and inserting in lieu thereof "National Heart and Lung Advisory Council".

REPORT TO CONGRESS

Review.

SEC. 8. The Secretary of Health, Education, and Welfare shall carry out a review of all administrative processes under which the National Heart, Blood Vessel, Lung, and Blood Disease Program, established under part B of title IV of the Public Health Service Act, will operate, including the processes of advisory council and peer group reviews, in order to assure the most expeditious accomplishment of the objectives of the Program. Within one year of the date of enactment of this Act, the Secretary shall submit a report to the Congress of the findings of such review and the actions taken to facilitate the conduct of the Program, together with recommendations for any needed legislative changes.

Ante, p. 680.

EFFECTIVE DATE

SEC. 9. This Act and the amendments made by this Act shall take effect sixty days after the date of enactment of this Act or on such prior date after the date of enactment of this Act as the President shall prescribe and publish in the Federal Register. Publication in Federal Register.

Approved September 19, 1972.

LEGISLATIVE HISTORY:

HOUSE REPORTS: No. 92-1108 accompanying H.R. 15081 (Comm. on Interstate and Foreign Commerce) and No. 92-1349 (Comm. of Conference).
SENATE REPORTS: No. 92-733 (Comm. on Labor and Public Welfare) and No. 92-1068 (Comm. of Conference).
CONGRESSIONAL RECORD, Vol. 118 (1972):
Apr. 7, considered and passed Senate.
July 18, considered and passed House, amended, in lieu of H.R. 15081.
Aug. 18, House agreed to conference report.
Sept. 6, Senate agreed to conference report.
WEEKLY COMPILATION OF PRESIDENTIAL DOCUMENTS, Vol. 8, No. 39:
Sept. 20, Presidential statement.

APPENDIX B
PLANNING EFFORT

In response to the legislative mandate, the National Heart and Lung Institute initiated an intensive planning effort in August, 1972 to formulate a National Program for accelerating the attack on heart, blood vessel, lung, and blood diseases and blood resource problems. The scope of this effort was strongly influenced by the 180-day time constraint imposed by the Legislation.

The objectives of this planning effort were to:

- Define the national problems in heart, blood vessel, lung and blood diseases and blood resources
- Assess the current state-of-the-art in these problem areas
- Identify new opportunities and approaches for present and future application
- Survey ongoing related programs in federal and nonfederal organizations
- Review and evaluate this information base and draw conclusions regarding national needs
- Develop recommendations for a National Program to solve these problems
- Develop a dynamic, flexible planning strategy
- Develop mechanisms for coordination of a National Program
- Develop an initial five-year plan for a National Program to accelerate the attack on heart, blood vessel, lung and blood diseases and blood resource problems.

To advise and assist in the formulation of the National Program, the NHLI relied heavily on the following groups and individuals:

- Approximately 300 Panel and Task Group participants, representing universities, medical schools, hospitals, and other parent institutions throughout the United States
- National Heart and Lung Advisory Council
- Interagency Technical Committee on Heart, Blood Vessel, Lung and Blood Diseases and Blood Resources
- Representatives of nonfederal and voluntary organizations with related programs.

The National Heart, Blood Vessel, Lung and Blood Program Committee (Figure B-1) and its four advisory Panels were established in August and September, 1972 to deal with the four major areas of the National Program:

- Heart and Blood Vessel Diseases
- Lung Diseases
- Blood Diseases
- Blood Resources.

The Panels subsequently organized 28 Task Groups (Figure B-2) to provide detailed scientific and planning data in major problem areas. The members of these Task Groups met in a nationwide, concerted effort over a period of several months to assess the current state-of-the-art in heart, blood vessel, lung and blood diseases and blood resources and to identify new opportunities and approaches. Important schedule milestones in the planning effort are identified in Figure B-3.

As a first step toward achieving the objectives leading toward an initial five-year plan for the National Program, the planning cycle depicted in Figure B-4 was initiated. A detailed description of each component of the planning effort is found in Figure B-5.

The initial results of this planning effort have been collected into a series of 37 information documents totalling nearly 9000 pages and summarized in Figure B-6. The Task Group efforts resulted in a comprehensive scientific base consisting of 28 unpublished Task Group reports—approximately 6500 pages. The complete set of Task Group reports represents an unconstrained inventory of current and potential research in heart and blood vessel diseases, lung diseases, blood diseases, and blood resources. These reports define major problem areas and specific problems. For each of the problems, they define approaches, and for each approach they define project areas. The information developed by the Task Groups from October through December includes identification of 39 problem areas, 78 problems, 400 approaches and 1868 project areas.

The project areas were categorized according to the major program objectives, as follows:

For the Disease Areas	For Blood Resources
• Prevention	• Supply
• Detection and Diagnosis	• Quality
• Treatment and Management	• Systems Effectiveness
• Rehabilitation	• Clinical Effectiveness

Additional information was also provided, such as approach objectives, present research status, research/technological inputs, key research events, significance and probability of success. Figure B-7 shows the distribution of project areas and approaches for each of the 39 problem areas in the data base generated by the Task Groups and demonstrates the wealth of opportunities for future programs.

The four Panels drew upon the Task Group data in preparing their respective Panel reports. The draft Panel reports were reviewed by the agencies represented on the Interagency Technical Committee, and by all bureaus, institutes and divisions of the National Institutes of Health, and their comments were taken into consideration in redrafting each report. The Panel reports summarize information from the Task Group data base, present the recommendations of the Panels and relate these proposals to the legislative requirements and the program objectives.

The four Panel Chairmen prepared a combined report, using as inputs the reports of the Panels and in consideration of the nearly 2000 project areas identified. Their report further refines the previous data base. It presents conclusions and gives priority recommendations in seven areas of heart, blood vessel, and blood diseases, in four areas of lung diseases, in four areas of diseases of childhood, and in seven areas of blood resources and transplantation.

In addition, the Panel Chairmen identified six general considerations common to all four Panels: needs for skilled manpower, education of the public, evaluation of new therapies, the development of better ambulatory care methods, demonstration projects and specialized facilities. They also considered whether they were applicable now, required further testing and evaluation before application, or required acquisition of new and basic information.

The National Heart and Lung Advisory Council received briefings on the development of the plan and reviewed the four Panel reports, the report of the Panel Chairmen, and selected Task Group reports. A special subcommittee of the Council was designated to draft their report, which was then reviewed and approved by the entire Council. It includes recommendations for an NHLI program with a five-year fiscal projection and requirements for staffing, and additional recommendations with regard to a number of general areas including education, control and prevention; scientists and their support; mechanisms of support; and construction.

During the planning effort, the NHLI also conducted an inventory of ongoing related programs in the NHLI, the other bureaus, institutes and divisions of the National Institutes of Health, other federal agencies and departments, and voluntary organizations. Information sources included: NHLI files; the Interagency Technical Committee; other bureaus, institutes, and divisions of the National Institutes of Health, supplemented by computer-stored information from the Division of Research Grants; and the Science Information Exchange of the Smithsonian Institution. This survey is presented in Volume V.

The NHLI Program Plan has evolved from the total information base generated in this planning effort in-

volving approximately 9000 pages of material as described above and summarized in Figure B-6. The Program Plan thus represents inputs from a variety of sources including the biomedical research community, the National Heart and Lung Advisory Council, the Interagency Technical Committee, other federal agencies, other institutes of the National Institutes of Health, and voluntary organizations with related programs. All of this information and advice has been retained as a comprehensive data base for further analysis and evaluation as the Plan continues to develop.

Figure B-1

NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM COMMITTEE

Chairman: Robert L. Ringler, Ph.D.

Heart and Blood Vessel Diseases Panel

Richard S. Ross, M.D., Chairman
Edgar Haber, M.D.
Robert Berne, M.D.
Paul Ebert, M.D.
Samuel Kaplan, M.D.
Lewis Kuller, M.D.
Henry McGill, M.D.
John A. Oates, M.D.
Louis Tobian, M.D.
Nanette Wenger, M.D.

NHLI Liasion:

Jerome G. Green, M.D.

Lung Diseases Panel

Eugene Robin, M.D., Chairman
Mary Ellen Avery, M.D.
Francis Chinard, M.D.
Benjamin Ferris, M.D.
Edward Gall, M.D.
James Hammarsten, M.D.
Alan Pierce, M.D.
Alexander Spock, M.D.
Robert Townley, M.D.
Gerald Weissman, M.D.

NHLI Liasion:

Claude J. M. Lenfant, M.D.

Blood Diseases Panel

Stanford Wessler, M.D., Chairman
A. B. Chandler, M.D.
William Connor, M.D.
Jerome Cornfield
Earl Davie, Ph.D.
Kenneth Moser, M.D.
Michael Mosesson, M.D.
Judith Pool, Ph.D.
Helen Ranney, M.D.
Samuel Rapaport, M.D.
Edwin Salzman, M.D.
Sol Sherry, M.D.
Louis Sullivan, M.D.
Harvey Weiss, M.D.

NHLI Liasion:

James M. Stengle, M.D.

Blood Resources Panel

Aaron Kellner, M.D., Chairman
Dennis Donohue, M.D.
Samuel Kountz, M.D.
Douglas Huestis, M.D.
Douglas MacN. Surgenor, Ph.D.
Scott Swisher, Jr., M.D.
Howard Taswell, M.D.
Frances Ward, Ph.D.

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Robert M. Pennington

Figure B-2

PANEL AND TASK GROUP ORGANIZATIONAL STRUCTURE

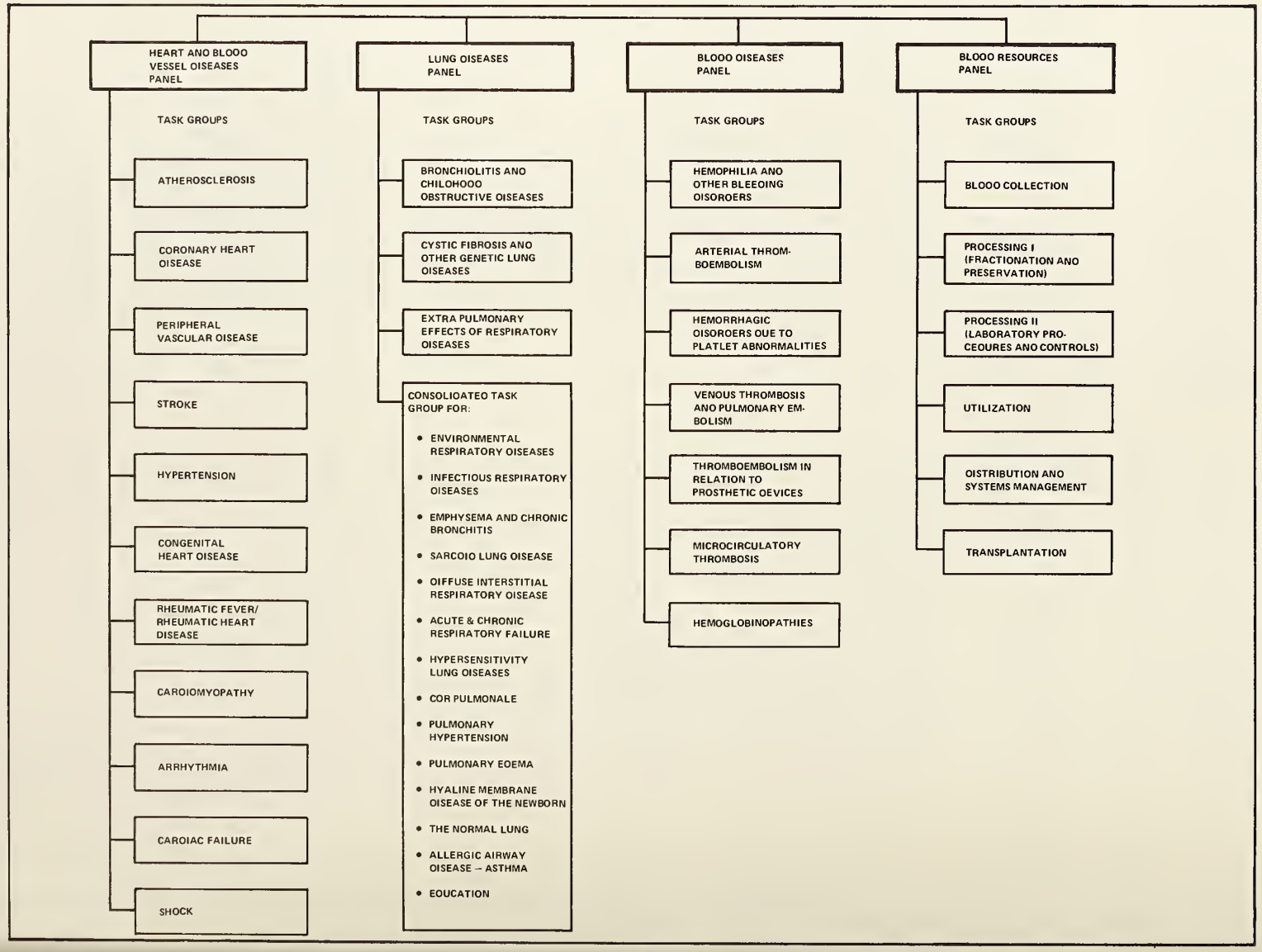


Figure B-3

SCHEDULE MILESTONES IN DEVELOPMENT OF NATIONAL PROGRAM

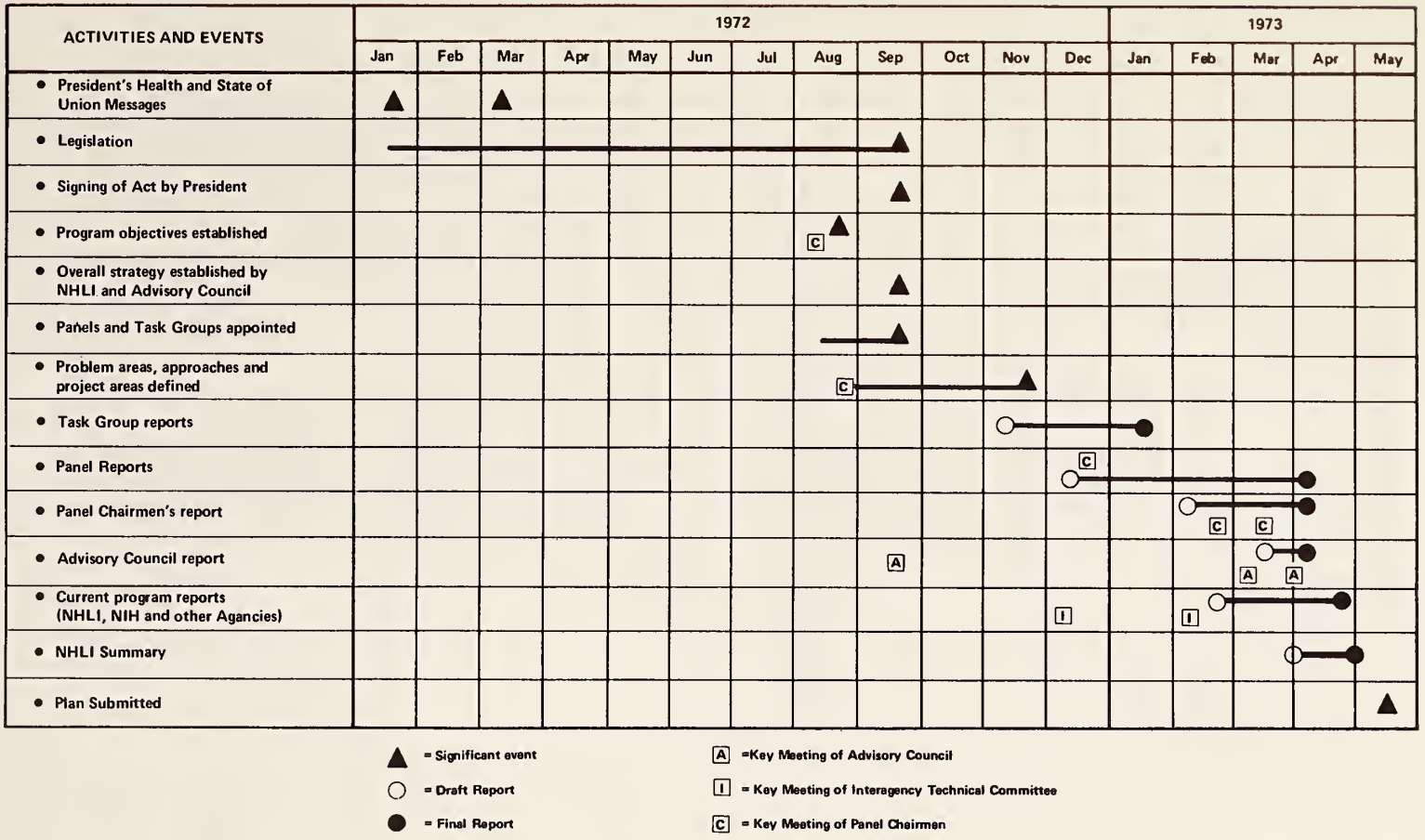


Figure B-4

THE PLANNING CYCLE

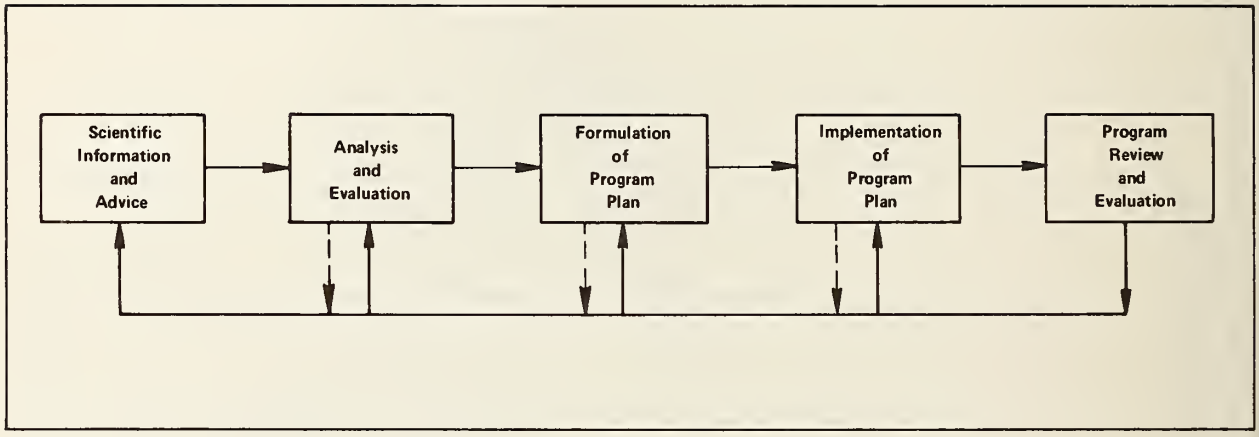


Figure B-5

COMPONENTS OF PLANNING EFFORT

SCIENTIFIC INFORMATION AND ADVICE	ANALYSIS AND EVALUATION	FORMULATION AND IMPLEMENTATION PLAN FOR A NATIONAL PROGRAM
1. Task Group Reports • approaches and project areas • summary and recommendations • supplementary data 2. Panel Reports • technical summary • recommendations 3. Report of the Panel Chairmen • priority recommendations 4. Report of the NHLI Advisory Council • priority recommendations • resource allocations • policy issues 5. Current Program Operation • correlation of current and proposed programs • program review and update procedures • implementation system	1. Program Impact Data • morbidity/mortality • cost/benefit 2. Priority Constraint Data • importance • feasibility 3. Logical Construction • gaps • overlap/duplication • interrelationships • sequence 4. Resource Allocation • personnel • equipment/facilities • historical cost data • cost projections 5. Program Balance • problems • goals • objectives • solutions • immediacy of application • interdisciplinary approaches • legislative requirements • dollars	1. Determine Major Problem Areas in: • heart and blood vessel diseases • lung diseases • blood diseases • blood resources 2. Select Programs to Attack These Problems 3. Justify These Program Selections 4. Determine Priorities Among These Programs 5. Project Resource Requirements 6. Plan Resource Allocation Scheme 7. Schedule Program Implementation 8. Organize for Implementation of Plan • overall management • program evaluation • dissemination of information to research community, public, the President and Congress • resource allocation policy: grants, contracts, intramural, centers, etc. 9. Plan for Coordination of National Program • National Heart and Lung Institute • Agencies represented on Interagency Technical Committee • Other nonfederal organizations

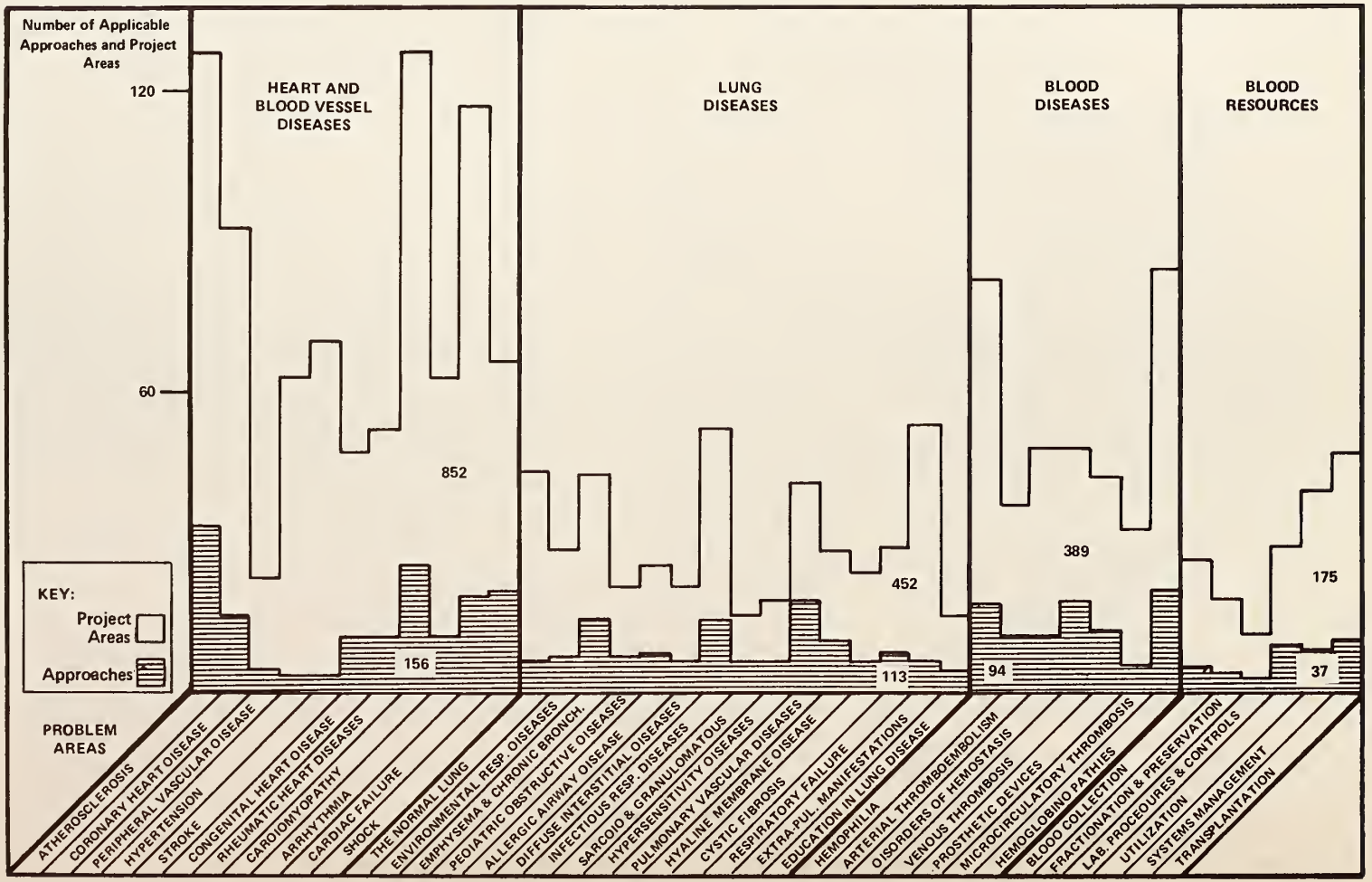
Figure B-6

INFORMATION BASE FOR THE NATIONAL PROGRAM

	INFORMATION COMPONENTS	INFORMATION DESCRIPTION	DOCUMENTATION		METHOD OF GENERATION	CONTRIBUTION TO PLAN
			NO. OF VOLUMES	NO. OF PAGES		
BIOMEDICAL RESEARCH COMMUNITY	TASK GROUP REPORTS	39 Problem Areas 78 Problems 400 Approaches 1868 Project Areas	28	6500	60 Planning Sessions	Comprehensive Identification of Research Needs
	PANEL REPORTS	Comprehensive Scientific Summary	4	1000		
	REPORT OF THE PANEL CHAIRMEN	Summary and Priority Recommendations	1	100	Three Planning Sessions	Program Priorities
COUNCIL ADVICE	REPORT OF THE NATIONAL HEART AND LUNG ADVISORY COUNCIL	Problem Area Priorities Resource Allocations	1	100	Regular Meetings Plus Special Subcommittee	Recommendations for Research Priorities Resource Allocations
RELATED CURRENT PROGRAMS	NHLI	Project Descriptions and Funding	1	400	Data Retrieval and Categorization	Baseline of Ongoing NHLI Research
	NIH (exclusive of NHLI)		1	400		Baseline of Ongoing Research in NIH (Exclusive of NHLI)
	AEC NASA DOD NSF DOT SRS EPA SSA FDA USDA HSMHA VA VOLUNTARY AGENCIES		1	400		Baseline of Ongoing Related Projects

Figure B-7

TASK GROUP GENERATED
DATA BASE



NATIONAL HEART, BLOOD VESSEL, LUNG AND BLOOD PROGRAM

VOLUME II

REPORT OF THE NATIONAL HEART AND LUNG ADVISORY COUNCIL

APRIL 12, 1973

NATIONAL HEART AND LUNG INSTITUTE/NATIONAL INSTITUTES OF HEALTH
U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

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I. INTRODUCTION

The National Heart, Blood Vessel, Lung and Blood Act of 1972 specifically states that the Director of the Institute, with the advice of the National Heart and Lung Advisory Council, shall develop a plan for a National Heart, Blood Vessel, Lung and Blood Disease Program. This report is the advice of the Council for such a program to advance the attack against these diseases and improve the management of the nation's blood resources.

The maturation of many research-proven ideas, methods and technologies, viewed in relation to the increasing health problems of heart, blood vessel, lung and blood diseases, convinces the Council that the next few years could bring significant new discoveries and health benefits for the American people. Great strides have been made in prevention, both real and potential, in diagnosis and in medical and surgical treatment of these major diseases. The result has been new hope for patients suffering from them. In fact, death rates from some of these diseases have levelled off or even decreased in the last few years.

The public deserves the fullest application now of the preventive, diagnostic and treatment measures already developed through research. At the same time, the research and clinical momentum generated in the unparalleled period of expansion of scientific medicine in the past two decades must be sustained, for it is through this momentum that important new knowledge will be generated and then translated into health benefits for all.

At the present time, the diseases addressed by the National Program together cause more than one million deaths each year in the United States. In their chronic forms, they affect more than 30 million Americans. The loss of productivity through disability alone is enormous.

Diseases of the heart and blood vessels are by far the largest problem. They account for more than half of the annual deaths from all causes in the United States (Figure 1), thus making this country's rate among the highest of the developed nations. Although the toll is heaviest in the older ages, a quarter of the deaths occur under age 65.

- Coronary heart disease, which includes heart attack, causes 675,000 deaths each year, many of which occur suddenly and unexpectedly; four million persons in this country have had a heart attack or suffer from angina pectoris.

- Every year 200,000 individuals die as the result of a stroke; 1.7 million persons are at least partially incapacitated from having suffered a stroke.

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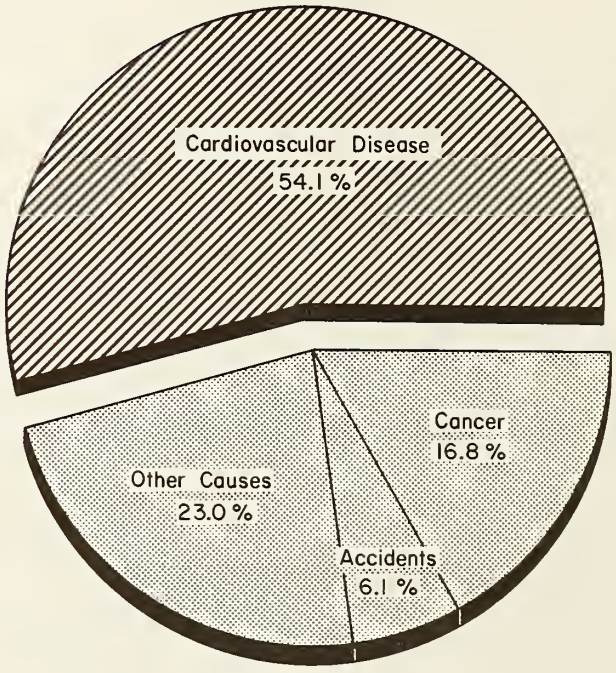
Figure 1

DEATHS FROM ALL CAUSES, UNITED STATES, 1967



- Hypertension, which predisposes to stroke and heart failure, affects 23 million Americans, 13 million under age 65.

If heart and blood vessel diseases could be eliminated as causes of death, the gain in life expectancy would approach 11 years, more than four times the gain that would be achieved by the elimination of any other cause of death.

The chronic lung diseases are also a serious health problem.

- Emphysema, chronic bronchitis and asthma afflict 14 million individuals, more than 11 million of them younger than age 65.

- Each year, emphysema, pneumonia and hyaline membrane disease kill 100,000 Americans.

Thrombosis and diseases of the blood are responsible for much acute and chronic disease.

- Venous thrombosis and pulmonary embolism strike 300,000 persons annually.

- Sickle cell anemia and hemophilia afflict 50,000 to 75,000 persons.

The impact of the heart, blood vessel, lung and blood diseases on the nation's economy is great. Each year, health expenditures for these diseases are more than $9 billion, and the value of present and potential earnings lost because of the illness and death they cause amounts to at least an additional $29 billion.

The Council believes that a plan for a National Program for the next five years will serve the following purposes:

- Provide a basis for decisions concerning appropriate support for needed efforts in the heart and blood vessel, lung and blood areas;

- Ensure proper priority and sequence of implementation;

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- Provide a basis for determining scientific manpower needs for research to sustain the total program;

- Facilitate coordination of the efforts of all Federal agencies in the heart and blood vessel, lung and blood fields;

- Make it possible to delineate Federal responsibilities so that state, local and private sectors can plan their participation and responsibilities accordingly;

- Enable orderly and systematic review and analysis of progress of the Program.

The Council believes that a National Program centered in the National Heart and Lung Institute is more appropriate than a variety of local programs. It should make possible a coordinated rather than an uncoordinated, fragmented effort, and should help to assure cooperation, communication and interchange of ideas and results among the many agencies, institutions and scientists involved in the total effort.

Within the framework of a National Program, priorities can be set and progress measured effectively. An analysis of progress undoubtedly will suggest modifications in the Program. A degree of flexibility must be maintained to accommodate changes.

The Council's report deals with the generation of new knowledge; the development of new diagnostic, treatment and prevention techniques and their evaluation; and the demonstration of their applicability. Although the Council addressed itself to matters of patient care and widespread application of diagnostic and treatment programs, it believes these matters can best be handled by other sectors of the private and public health care establishment. However, the Council recognizes that the National Heart and Lung Institute must interact regularly and systematically with other agencies responsible for health care in order to assure the most timely and effective application of the results of its work.

The Council believes that much attention must be devoted to developing the nation's health resources. One example is an urgent need for a blood bank program to husband this vital resource. The Council believes that scientific knowledge is also a major national resource and, more importantly, one which should be immediately available to people in all the states of the nation. An adequate system for dissemination of information could accomplish this purpose. The development of these and other national resources to benefit the health needs of the nation presents a real opportunity and challenge.

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II. GOALS

The immediate goal is to secure the additional knowledge and techniques needed for early diagnosis and effective treatment of existing disorders of the heart, blood vessels, lungs and blood and to demonstrate their application to the health care problems of the country. The long-range goal is prevention and elimination of disease. Before presenting specific high-priority programs, the Council believes it is important to state clearly the lessons we have learned about scientific discoveries necessary to solve the great problems of these diseases.

First, although we have learned much about the heart and blood vessels, lungs and blood, our areas of ignorance are still far greater than areas of complete understanding. The following are but a few examples:

- In the past three decades, we have learned how to prevent rheumatic fever and rheumatic heart disease by treating the antecedent streptococcal infection with penicillin. For those patients who developed rheumatic heart disease before that time, we have learned how to repair or replace badly damaged heart valves. But we still do not know how to ensure that every child with a sore throat has a throat culture or how to treat all susceptible children long enough to prevent heart disease.

- In the past three decades, we have learned how to use new drugs to lower blood pressure in hypertensive patients to lessen the risk of strokes and heart failure. But we still do not know what causes most forms of high blood pressure, how to motivate the population to be screened for high blood pressure, or how to initiate and maintain effective therapy in all those with high blood pressure.

- We have learned how to catheterize the hearts of small babies to identify congenital heart lesions, and how to correct them by open heart operations. But we do not know how many congenital cardiac defects are genetic or how many reflect the environment of the fetus, and, except for some defects known to be due to rubella virus, we do not know how to prevent congenital heart disease.

- We know how, by surgical procedures, to correct or by-pass atherosclerotic obstructions in the arteries. But we do not know how to prevent atherosclerosis or how to diagnose and treat it early.

- We have sophisticated physiological tests that tell us precisely the functional defects of diseased lungs. But we do not know the cause of pulmonary emphysema, how to stop its progress even if detected early, or how to prevent heart disease caused by emphysema.

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- We know the specific clotting factor whose deficiency causes hemorrhage in patients with hemophilia. But to treat these patients requires harvesting the factors from more than 50 percent of the national blood supply. We do not know how to obtain these factors with reasonable cost-effectiveness; neither have we discovered alternative treatments.

We tend to obscure our ignorance by making it seem that a problem has been solved when it has, in fact, been only half solved. We must face up to our ignorance in many matters and recognize that an entirely different type of knowledge than we now have will be necessary to fully solve these problems.

Second, by far the surest way to save the public's health dollar in the long run is to obtain a clear enough understanding of the mechanisms causing heart, blood vessel, lung or blood diseases to permit prevention or complete cure. The less we know about a disease, the less specific is the treatment and the greater the cost. Specific prevention and definitive treatment usually cost relatively little and are easily translated into effective action.

- Twenty-five years ago, all we could offer patients with tuberculosis was nonspecific sanatorium or surgical care which was very costly and not very effective. We now have specific chemotherapy; it is both effective and cheap.

- Finding factors that produce rheumatic fever and a way to prevent rheumatic heart disease have proved to be far less costly than modern diagnosis and surgical treatment of patients with damaged heart valves.

- It is far less expensive to provide rubella vaccine to future mothers before their child-bearing age than to perform heart surgery to correct the congenital heart defects that rubella causes.

In the long run, investment in fundamental and clinical research to learn the mechanisms and causes of diseases and to prevent them has been far less expensive than paying for half-way measures, the results of which can only be a reduction in disability.

Third, to bring the best possible health care to the people of our country and, ultimately, to prevent disease, we must accelerate two campaigns: (1) to apply what we now know as effectively as we can, and (2) to gain new knowledge and new understanding—of the basic biological processes and mechanisms underlying normal heart, blood vessel, lung and blood functions; of the biochemical, genetic, nutritional, behavioral, social, environmental and other processes that lead to diseases of these systems; and of ways to prevent or counteract these diseases.

Both campaigns are essential. We cannot tell patients who are ill with a disease that we are concerned only with the prevention of such disasters in others; for them, having the best available treatment may be a matter of life or death. We must not have all basic research and no applied; but neither must we have all applied research and no basic. Neither should these campaigns be sequential. We cannot double applied research and stop basic research for five years and then double basic research and stop applied research for five years.

Fourth, contrary to popular conception, it can be documented that important new knowledge rarely comes through sudden "breakthroughs"; research goals are almost invariably reached by a steady accumulation of knowledge—bit by bit—until finally the last bit secures a major advance. In biological research, crash programs often crash!

Similarly, great clinical advances rarely burst upon the scene as the result of mission-oriented, commission-directed programs, but come at a logical time when a broad advance in basic biologic science (often not directed toward the prevention or treatment of a particular disease) has made the clinical discovery nearly inevitable. Mission-oriented programs can then accelerate the achievement of the final specific goal.

One of the most important and certainly the most dramatic advances of the past two decades has been the development of open heart surgery. To the lay public and to many physicians and scientists, open heart surgery stands out as a great achievement of mission-oriented, goal-directed research. And it is true that the development (by mission-oriented research) of a pump-oxygenator was absolutely essential to open heart surgery. But it is crucial to the understanding of scientific discovery to realize that the development of a pump-oxygenator was itself possible only because of many earlier discoveries that were not mission-oriented, such as:

- Discovery by a physiologist of heparin, a substance that prevents blood clotting;

- Discovery by an immunologist of blood groups that led to blood typing and safe blood transfusions (and today to safe blood use in pump-oxygenators);

- Studies of red blood cells, their natural lifespan and how to preserve their life outside the body—which led to the storage of blood for emergencies and then to blood banks;

- Studies by biochemists on the diffusion and exchange of oxygen and carbon dioxide, essential for construction of artificial oxygenators.

But successful open heart surgery required more than a pump-oxygenator. It also required accumulation of considerable knowledge in many biologic fields. It had to await basic research on the heart's conducting system and on arrhythmias that led to devices to control serious arrhythmias; on fluid and electrolyte metabolism that permitted long surgical procedures; and on anesthesia, respiratory physiology and mechanics of ventilation that permitted proper ventilation and anesthesia of a patient with an open chest. Other important contributions were the discovery of the electrocardiograph, of hypothermia, of techniques for electively stopping and restarting the heart, and of chemotherapy and antibiotics.

Knowledge flows in both directions. Thus, the identification and study by surgeons of new problems in patients who have undergone open heart surgery stimulated renewed research efforts and produced new knowledge in basic research in many fields.

A recent analysis of 175 scientific discoveries that had to be made to permit the great clinical advances of the 1950's and 1960's in the treatment of heart, blood vessel, lung and blood diseases, showed that 36 percent were basic discoveries completely unrelated to these diseases; 31 percent were made in basic research designed to contribute to solution of a clinical problem; and 33 percent were made as a result of applied mission-oriented research. Therefore, an essential part of the Council's philosophy is that both applied science (and development and engineering) and basic science are essential. The Council hopes that the public will come to recognize that the *last event* leading to a dramatic clinical advance is possible only because of scores or hundreds of earlier discoveries. We should not talk in terms of supporting either basic *or* applied, or targeted *or* nontargeted research. We must support mission-oriented research to alleviate suffering and reduce disability and we must support nontargeted research to uncover knowledge not yet imagined by the most competent commissions, panels or task forces appointed by public or private agencies.

Fifth, the all important clue to the cause and prevention of atherosclerosis or emphysema, as well as many other diseases, may come from scientists working in an unrelated field.

- When Karl Landsteiner discovered human blood groups, he was investigating basic problems in immunology; he was not then aware he was making safe blood transfusion possible.

- When Roentgen discovered X-rays, he did not realize it would enable physicians to visualize the heart, lungs, and blood vessels of their patients.

- When Cournand and Richards passed a catheter into the heart of a man, it was not to develop methods of diagnosing congenital or acquired heart disease; they wanted to measure the oxygen in mixed venous blood to learn more about basic physiologic problems of pulmonary gas exchange.

- When Alexis Carrel developed the new science of suturing blood vessels and transplanting arteries, veins and whole organs, it was a necessary first step to his main goal of studying basic life processes and the metabolic requirements of each organ for optimal function.

- When Davies and Brink devised an "electrode" to measure the oxygen used by nerve cells, they had no idea that it would become an essential monitoring device in every intensive care unit for measuring blood oxygen.

These examples make it clear that a successful effort against heart, blood vessel, lung and blood diseases will depend, in part, upon strong and sustained support of basic and mission-oriented research in other fields of science, as well as those fields directly concerned with these diseases.

III. PREVENTION, DIAGNOSIS AND MANAGEMENT OF SPECIFIC DISEASES: RECOMMENDATIONS

Late in 1972, a Committee consisting of four Panels—one each for heart and blood vessel, lung, and blood diseases and a separate one for blood resources—was established to assist in the formulation of a coordinated plan for a National Heart, Blood Vessel, Lung, and Blood Program. These consultant Panels, with the help of approximately 250 additional medical and scientific advisors, assessed present knowledge and identified areas in which progress against heart, blood vessel, lung and blood diseases may be expected or is urgently required. The following four sections are the Council's evaluation of the four separate Panel Reports and the summation by the Panel Chairmen.

As indicated in each Panel Report, there are many urgent problems in each disease area. The Council believes that proper application of existing knowledge now would decrease illness and death from heart and blood vessel, lung and blood diseases. At the same time, however, there is need for new knowledge and for the entry of this new knowledge into the management of disease. A nationwide, coordinated effort to exploit our present understanding, to remedy current inadequacies, to seek new knowledge, to develop new techniques, and to establish new directions of inquiry seems particularly timely.

1. HEART AND BLOOD VESSEL DISEASES

Heart and blood vessel diseases have been the major cause of death in the United States since the 1920's. Although there has been a decline in death and disability attributable to rheumatic fever, hypertension and stroke, the overall rate for all heart and blood vessel diseases is still 54 percent of all deaths in the United States.

- Atherosclerosis, including coronary heart disease and stroke, accounts for more than 800,000 deaths each year.

- Hypertension, although not a common direct cause of death, affects about 10 percent of the total population of this country and about 30 percent of the black population.

The Council concurs with the conclusion of the Heart and Blood Vessel Diseases Panel that, in the long run, the most rewarding approach will be the development of more effective methods for the prevention of heart and blood vessel diseases based upon a better understanding of the mechanisms of specific disease entities.

Atherosclerosis

Atherosclerosis is a slowly progressive, long-term disease that probably starts in childhood. It may produce no symptoms and, therefore, go undetected for years but eventually may result in a heart attack or stroke. Although many factors—such as elevated blood lipids, hypertension, and cigarette smoking—probably contribute, how atherosclerosis develops is not understood. Further, studies of its natural progression are

sharply limited in effectiveness because there is no simple way of detecting it until the arteries become so narrowed that painful symptoms result from the decreased blood supply, or until the formation of a blood clot (thrombosis) suddenly occludes an artery causing a heart attack or stroke.

The Council gives highest priority to understanding the basic mechanisms of atherosclerosis through studies of the cellular biology of the blood vessel wall and its interaction with circulating blood and its components.

The Council also emphasizes the need for development of simple, noninvasive techniques for detection of asymptomatic atherosclerosis.

Intervention trials, such as modifying diet, stopping smoking, controlling hypertension, and improving physical fitness, now must go on for many years because they must use as end points the occurrence of such events as heart attacks and strokes. Faster, more economical, and more definitive clinical trials would be possible if simple methods for detection were available.

Clinical intervention trials need to be conducted, and because current end points are crude, they will require large numbers of subjects studied over long periods if meaningful results are to be obtained.

Thrombosis

Thrombosis—the formation of a clot in a blood vessel—is intimately related to atherosclerosis. It not only contributes to the progression of the atherosclerotic lesion but also is responsible for many of the clinical complications of atherosclerosis. It may occur suddenly on an atherosclerotic plaque, causing severe or total occlusion of a blood vessel to the heart or brain, thus resulting in a heart attack or stroke. The reason for this sudden localized clotting of blood is not known.

Knowledge of how thrombosis is initiated and propagated within atherosclerotic and normal blood vessels will allow design of new therapy. This knowledge can be gained by studies of the clotting process, the wall of the blood vessel and the dynamic properties of flowing blood.

The Council believes that studies of the mechanism of thrombosis would contribute to reducing the high morbidity and mortality resulting from atherosclerosis.

Thrombosis not only affects man's own vessels, but it also limits the usefulness of vascular prostheses and is a serious barrier to the development of long-term circulatory assistance or replacement devices (see page 15).

Coronary Heart Disease

Under the broad heading of atherosclerosis, atherosclerosis of the coronary vessels is the major problem. Two aspects in particular require special attention—myocardial infarction and sudden death.

Myocardial infarction irreversibly damages heart muscle, and, if extensive, causes heart failure, either during the acute episode or following recovery from the attack. Means to reduce the amount of damaged muscle would substantially reduce the threat of heart failure and reduce the disability following a heart attack.

One half or more of the deaths from coronary heart disease occur suddenly. Current evidence suggests these deaths probably result from arrhythmia (abnormal heart rhythm) or cardiac arrest. How to prevent or treat such events represents a major problem in heart disease today. If the patients likely to develop these fatal arrhythmias could be identified, many lives could be saved by appropriate preventive or resuscitative procedures.

The Council recommends broad studies, by a variety of approaches, of means to minimize the mass of irreversibly damaged tissue resulting from occlusion of the coronary vessels.

The Council recommends continued exploration of the electrophysiology of the heart in order to develop more effective antiarrhythmic drugs.

The Council recommends studies to identify the population at risk of developing arrhythmias so that prospective therapeutic trials aimed at prevention can be designed and initiated.

Hypertension

Hypertension can be controlled by a wide variety of drugs, but they must be taken continuously for the

remainder of the patient's lifetime. Current treatment is empirical and only a few types of hypertension are curable because in only a few types is the cause understood.

The Council gives high priority to investigation of the causes of hypertension through studies of all the physiologic control systems that determine arterial pressure.

Such knowledge will have two benefits: (1) it will allow development of specific treatments to replace the empirical ones now used; this is of particular importance because of the possibility of long-term side effects, as yet unrecognized, if patients must continue indefinitely on drugs, and (2), such knowledge may allow development of methods to cure hypertension.

Recent work has shown that control of high blood pressure by drugs substantially reduces the likelihood of strokes and heart failure, but a similar beneficial effect on the occurrence of heart attacks has not yet been demonstrated.

The Council recommends continuation of clinical trials to determine the effect of long-term treatment of mild-to-moderate hypertension on the incidence of strokes and heart attacks.

Rheumatic Fever and Rheumatic Heart Disease

The relation between streptococcal infection and rheumatic fever is well established, and prevention of rheumatic heart disease is near attainment. To achieve this goal, continued efforts should be directed toward developing a vaccine for active immunization against streptococcal infection. Such a vaccine would eliminate the necessity for life-long treatment with antibiotics. It is also important to determine why rheumatic fever develops only in some people with streptococcal infections, why rheumatic heart disease develops in only a proportion of people who develop rheumatic fever and why it selectively damages heart valves.

Until the final goal of prevention is reached, emphasis must be placed on early recognition and treatment of streptococcal infections, on behavioral research into the motivation of parents and children to seek immediate diagnosis and to stay on continued long-term treatment programs, and on improvement of techniques to facilitate rapid culture of streptococci.

Congenital Heart Disease

At the present time, surgical correction of most congenital heart defects is possible. The Council is convinced, however, that prevention of congenital heart defects should be an ultimate goal of the National Program.

The Council recommends an intensive interdisciplinary study of the neonatal heart and blood vessels and all aspects of the etiology and pathophysiology of congenital heart disease.

Because the majority of deaths occur during the first days or weeks of life, early recognition and treatment are the essence of an effective program.

The Council recommends efforts be made to improve early recognition and facilitate prompt treatment of infants with congenital heart disease (see page 20).

Heart Failure

Heart failure is a serious complication of heart attack which may develop during or after the attack; it is also an important manifestation or consequence of a variety of diseases affecting the function of the heart, including hypertension, and rheumatic and congenital heart disease.

Current treatment is still either empirical or directed at secondary manifestations, such as edema. New information is needed concerning cardiac function in order to design improved therapy for patients with heart failure, whatever the cause, and to investigate new methods of prevention.

The Council gives priority to studies of the contractile process and development of methods to improve the function of heart muscle, and to studies of the humoral, neural, and endocrine factors which are involved in normal and abnormal cardiac function.

2. LUNG DISEASES

The Report of the Lung Diseases Panel testifies eloquently to the disparity between the large number of severe lung disease problems and the few basic biologic facts available with which to fashion relevant therapy and prevention. The Panel Chairman, in presenting his report to the Council, commented on this disparity: "Study of respiratory diseases has only recently moved

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out of the tuberculosis sanitaria." Until recently, most pulmonary research concerned the lung as a site for infectious disease. The first textbook of lung physiology was published as recently as 1955 and subsequently the lung was studied primarily as a gas exchanger. Only in the last five years has the lung been studied as an organ with specific problems and properties.

As a public health problem, lung diseases are very important:

- Asthma affects 9 million Americans and usually lasts for years.
- Emphysema and chronic bronchitis doubled in incidence between 1958 and 1967. In 1967 they cost the U.S. economy an estimated $1.2 billion. Unlike most other diseases, they continue to increase.
- Lung fibrosis and respiratory failure are now being recognized in larger numbers—due in part to improved techniques of recognition and in part to environmental factors. Mortality in respiratory failure approaches 40 percent.
- Hyaline membrane disease affects about 50,000 newborns annually. Due to recent research advances, the disease is usually diagnosed correctly but survival varies from 20 percent in the majority of hospitals to 80 percent in a few excellent centers.

In contrast to the great and increasing problems of lung disease, there is a dearth of basic knowledge about the lung. The Lung Diseases Panel Report details many basic questions about the normal and diseased lung which must be answered as soon as possible if reduction in morbidity and mortality of lung diseases is to be accomplished.

The Lung and its Biology

Faced with this large discrepancy between severity of disease and lack of basic knowledge, the Panel Chairmen responded with the following general recommendation:

> "The major missing element in those respiratory diseases which comprise the bulk of respiratory disease is knowledge of the cellular biology of lung tissue. Understanding of this area would lead to major advances in chronic bronchitis, emphysema, pulmonary fibrosis, immunologic lung diseases, respiratory diseases of children and respiratory failure. Hence, studies in this area are the number one priority. More rapid progress in this area would be made by the establishment of investigative units organized to explore these basic considerations."

The Council strongly supports the Panel's recommendation. The priority need is for basic research into the lung and its biology.

Any other approach would be palliative and eventually would emphasize the status quo. Research now in progress is expanding rapidly in areas such as normal lung metabolism, function and development, study of lung cells, response of lung to air pollutants and the basic chemical nature of the elastic fabric of the lung which is lost in diseases such as emphysema. Because research in lung biology and lung diseases is only beginning to emerge, extra efforts must be made to attract and support good investigators—young and old—in this area. Otherwise, programs will be seriously understaffed and progress will be limited.

Emphysema and Chronic Bronchitis

The Council recommends that an attack be mounted on emphysema with major emphasis on an intensive effort to find the cause of this important disease.

All possible causes should be identified and systematically studied or eliminated. Particular attention should be paid to the reaction of the lung to injury by physical and chemical agents, infectious diseases, metabolic diseases and reduced blood supply, and the mechanisms by which the lung defends itself. Advances in understanding the lung in emphysema, the principal clinical problem in pulmonary disease, will at the same time provide much basic data needed for further progress in other areas.

At all times, methods for early diagnosis and methods to prevent emphysema or halt its progress should be sought. As an example of a specific approach, programs designed to decrease smoking would have a major impact. The reduction of smoking in the young would be a preventive measure and at the same time would yield valuable prospective data on the effect of smoking on development of chronic lung and heart and blood vessel diseases (see also page 20).

Respiratory Failure

The Council believes that immediate improvement in the problem of respiratory failure is possible through increased emphasis on clinical studies, improved early detection, and demonstration of emergency services, especially intensive respiratory care research units. For the long-range attack on this problem, basic knowledge of the pathophysiology of the condition through animal study should be encouraged.

The development of an artificial lung to support adults and infants in respiratory distress is now underway. This effort should be vigorously pursued for such a device would provide both clinical benefits to patients and new capabilities in the research laboratory.

Immunologic Lung Diseases

Several lung diseases are a consequence of immunologic abnormalities. They include asthma, hypersensitivity pneumonitis, sarcoidosis and lung fibrosis. A rationale for treatment of immunologic lung disease will require an understanding of immunologic differences between various individuals and between the elderly and the young.

The Council believes that basic studies of the immunology of the lung are required.

Studies are needed to identify the causes of pulmonary fibrosis and sarcoidosis and to elucidate the role of infection in causing an asthmatic attack.

Lung Diseases of Infancy and Early Childhood

The Council concurs with the following Panel Chairmen's recommendation:

"Hyaline membrane disease and cystic fibrosis require the development of methods of early and prenatal diagnosis and the development of regional emergency care centers where meticulous and sophisticated techniques are available, including provision for rapid transfer of affected children to these facilities."

Prospective, controlled studies of infants likely to develop hyaline membrane disease are indicated (see page 20). Recent research offers an explanation of why infants born prematurely may develop this disease and provides methods for detection of risk prior to birth. As an immediate measure, prenatal detection and therapy must be evaluated and presently defined criteria for treatment must be standardized to assure optimal care and survival. Such studies can best be carried out in a small number of specialized centers of research. The concept of these centers is developed below (see page 30).

The goal of prevention will require basic understanding of the cellular biology of the developing fetus and the control mechanisms of fetal maturation. Furthermore, understanding of the basic mechanisms responsible for premature birth is essential in order to prevent premature delivery and thereby reduce the incidence of hyaline membrane disease. This disease demonstrates very well how ultimate control of disease rests upon the understanding of its basic cause.

Obstructive Lung Diseases in Infants and Children

The Council recommends studies to define the causes of upper and especially lower airway obstructive disease in children.

It is important to determine whether obstructive lung disease in children predisposes to the development of obstructive lung disease in adults. Investigations of croup and bronchiolitis should be directed toward determining their cause and developing methods for early detection and specific management. Emphasis should be on epidemiological and long-term follow-up studies.

In much the same way that the problems of infants with hyaline membrane disease might best be served by specialized centers of research, obstructive lung disease in children should also be studied in such centers.

Manpower Needs

The Panel pointed to manpower needs in the area of lung diseases. Because of the markedly increased emphasis on lung diseases and the magnitude of the clinical problems, the demand for trained manpower is greater than the supply. More than 200 vacancies for trained investigators and clinicians exist at present. This is one of the major examples of our failure to apply current technology consistently for every patient needing it. The limiting factor is quite simply

the small national pool of trained and knowledgeable personnel. Plans for meeting these immediate and future needs must be implemented at once to prevent a critical shortage of manpower.

3. BLOOD DISEASES

The Blood Diseases Panel Report addressed three principal areas as follows:

- *Thrombosis,* with emphasis on two major aspects: (1) arterial thrombosis and its role in causing such serious and fatal complications of atherosclerosis as heart attacks and stroke, and (2) venous thrombosis and pulmonary embolism.

- *Hemorrhage,* with emphasis also on two major aspects: (1) the seriousness of uncontrolled hemorrhage, a major cause of morbidity and death, in a variety of conditions, such as after surgery or accidents or in cirrhosis of the liver; and (2) the hemophilias, inherited hemorrhagic disorders which have great socioeconomic consequences, on families with these diseases and on society generally, particularly on the blood resource system of the country.

- *Sickle cell anemia and related inherited disorders* of the red cell and its contained hemoglobin.

Many significant advances have been made in the treatment of certain thrombotic and hemorrhagic diseases; research discoveries have become part of everyday medical practice. Examples include anticoagulant therapy for patients with clotting problems and plasma concentrate treatment for hemorrhage in hemophilia. But many serious disorders cannot be prevented or treated effectively, or at times even diagnosed. For example, thrombosis may go entirely undetected until the clot or a piece of it breaks loose and causes a sudden catastrophe such as pulmonary embolism or gangrene of an extremity.

By the authority of the National Heart, Blood Vessel, Lung, and Blood Act of 1972, not less than 15 percent of the funds appropriated to the National Heart and Lung Institute shall be reserved for "programs respecting diseases of the blood." An important segment of the program relates to sickle cell disease. Initiation of this activity was accompanied by specially earmarked funds. These funds, together with sizeable annual increments in the funding level, have made it possible to implement an effective sickle cell disease program which should continue. Other disorders of the blood likewise disable or cripple many thousands. These diseases could be expected to yield to intensified attack, sparing patients pain while conserving the nation's blood resources as well. Concentrated research effort directed toward specific blood diseases is essential and overall program balance is needed. The following paragraphs present the Council's recommendations in the area of blood diseases.

Pathogenesis of Blood Diseases

The Council concurs with the Panel's recommendations that a major effort should be made in research on the pathogenesis of thrombosis **(see page 10).**

The Council recommends that a major effort should also be made on the pathogenesis of hemorrhagic diseases and red cell diseases and the biologic mechanisms underlying these disorders.

Basic knowledge is urgently needed on the mechanisms of blood clot formation, thrombus formation on atherosclerotic plaques, and prevention of thrombosis. Treatment of the thrombotic disorders, based on present knowledge, can be only partially effective at best.

Additional basic information in molecular genetics could completely alter the approach to treatment of the inherited blood diseases, hemophilia and sickle cell anemia. For example, if one could "turn on" the latent capacity of the sickle cell anemia patient to produce normal fetal hemoglobin, the scourges of this disease could be largely overcome.

Clinical Trials of Antithrombotic Agents

There are many drugs today which may prevent or dissolve clots, such as the coumarins, heparin, the thrombolytic agents, aspirin, and certain snake venoms. Special attention is required in the selection of appropriate drugs for clinical trial.

The Council believes that clinical trials of promising new drugs should be conducted.

The Council agrees with the Panel Chairmen's recommendation that aspirin and low dosage heparin as antithrombotic agents are the most promising candidates for testing at this time. Other possible agents are the antithrombotic snake venoms and the thrombolytic agents. However, end points for determining efficacy may be especially difficult. Careful design of the studies must take into account rigorous assessment of feasibility, present state of the art, and cost versus probable knowledge to be gained. Also, the problems

that may be encountered in translating the findings to general medical practice should be considered before starting any clinical drug trials.

Development of Nonthrombogenic Surfaces

Completely satisfactory materials for heart valves, artificial organs, and other prostheses are not available. All of those presently in use stimulate the formation of thrombi.

Greater emphasis, in both applied and basic research, should be given to nonthrombogenic surfaces.

Research is needed on the surface characteristics of biomaterials, as well as on the normal lining endothelium of the blood vessels. The former are thrombogenic, the latter is not. Elucidation of this difference could result in development of completely nonthrombogenic surface materials and of ways to avoid thrombi in thrombosis-prone diseased vessels.

4. BLOOD RESOURCES

The availability of an adequate supply of high-quality blood and blood products is essential for effective treatment of many diseases. The report of the Blood Resources Panel deals with four important areas: A National Blood Bank System, Blood Component Therapy, Hepatitis, and Transplantation Immunology.

In the assessment of priorities and opportunities in the blood resources area, a number of factors were considered, including the following:

- The magnitude and strength of the diverse but uncoordinated blood banking system which presently functions to meet most medical situations, but whose many defects could be overcome with a well-coordinated national system;
- The inadequacy of present blood fractionation methods and the need for vigorous attention to more efficient isolation of the many cellular and plasma components of the blood; and
- The fact that rapid advances are being made in understanding hepatitis, including serum hepatitis, but there is still no way today to ensure that blood from a given donor will not transmit the disease.

A National Blood Bank System

A national blood bank system should be developed from existing blood bank resources of the country so that a coordinated system based on regions would eventually result. Part of this effort would include the establishment of a national blood data center and a continuing campaign on the national level for recruitment of blood donors to ensure an adequate supply of blood for the country's needs. The system could eventually include preservation and storage of organs and tissues for transplantation.

The Council believes a coordinated blood bank system at the regional and national level is highly desirable, provided that full utilization is made of the existing resources in present blood banking organizations.

The blood bank system should include the supply of blood, its processing, distribution and utilization. It could also included tissue typing and organ preservation but not other aspects of transplantation.

The role of the National Heart and Lung Institute should be to facilitate coordination and further development of present resources into a total national program. No single rigid pattern of organization would likely meet the diverse geographical requirements of the country.

The deficit in trained personnel deserves special attention. Training of professionals in the blood banking field is very limited in this country and is inadequate to meet the demands for qualified physicians to staff the blood banks of the nation.

Blood Component Therapy

Blood component therapy, to be fully effective, requires improvement in blood cell preservation and plasma fractionation, so that the many important components of blood such as platelets, immune globulins and antihemophilia factors can be fully recovered for treatment purposes.

The Council emphasizes the need for improved therapy using blood cells, particularly white cells and platelets, and plasma protein components.

Specialized centers of research in blood and blood resources should be established.

Competition for the specialized centers should be on a broad base and not limited solely to regional or national blood centers. One or more of these centers should contain pilot plants to develop and test new methods for plasma fractionation. Fundamental research in immunology, immunogenetics, and other aspects of transplantation biology could be carried out in such specialized centers although clinical trials of organ transplantation would not be appropriate until fundamental new knowledge is available.

Hepatitis

Hepatitis, which includes hepatitis B transmitted by blood transfusions, continues to be an important public health problem, requiring a coordinated attack.

The Council recommends continuation of studies aimed at better understanding of the virus, improvement of tests for detecting carriers of the disease, and development of a vaccine.

Transplantation Immunology

Transplantation immunology requires continued research and development if wider and fully successful use of organ transplants in the heart and blood vessel, lung and other areas is to be realized.

General Comments

In the operational area of blood banking, the role of the National Heart and Lung Institute should be that of catalyst for the system, through collection of data, support of research and development in the blood area, and provision of a meeting ground and advisory system to the purveyors of blood and blood derivatives in the country.

Motivational research is needed to understand more fully the reasons that prompt people to give blood, in order to place the blood donor recruitment system on a sounder basis (see page 17).

There must be a continuing program for professional and public information and education regarding blood and its most effective utilization. In addition, special efforts must be made to enlist the interest of the scientific community in the blood resources field so that more attention is given to important research and development leading to better utilization of our blood resources (see page 19).

5. GENERAL NEEDS FOR ALL AREAS

Certain common needs are shared by all four areas—heart and blood vessel diseases, lung diseases, blood diseases, and blood resources—discussed in this report. Among these are information gained from studies of genetic factors, animal models and human motivation.

Genetics

There is firm evidence that hypertension is, in part, an inherited disorder. Atherosclerosis may also have genetic determinants. Hemophilia, sickle cell disease and thalassemia are definitely inherited disorders. In a small proportion of patients with emphysema (those with the alpha$_1$-antitrypsin deficiency), a genetic defect is present.

It is clear that knowledge concerning genetic factors is necessary not only for understanding how diseases develop but also for the design of specific treatments. Such information could come from study of human populations as well as from study of animal models of human disease.

The Council recommends that a strong and positive program of genetic research and counseling be established to help decrease heart, blood vessel, lung and blood diseases of genetic origin.

Animal Models

Use of animal models can have important impact on understanding disease and often may be the only available research approach. For instance, recognition of a naturally occurring hemophilia in dogs allowed identification of the causes of this disease. Development of models of thrombotic and other hemorrhagic diseases is needed. Animal models of hypertension, developed by a variety of different methods, have shown the multifactorial nature of this disorder and have improved the development of drugs for treatment. Our understanding of atherosclerosis would be much advanced by the availability of a primate model which would allow application of current knowledge in design of methods of control and which could be used as new leads develop. Similar benefits would accrue from the development of animal models of lung diseases.

Motivational Research

Very little is known about the factors that motivate individuals to help or hinder control of their health problems. For example, cigarette smoking is known to cause lung disease; the information has been widely disseminated, but cigarette usage has risen. Hypertension is now controllable by drugs, yet a substantial number of patients do not seem willing to continue the necessary long-term treatment. Some types of hyperlipidemia can be easily controlled by simple dietary modification, but many people either will not or cannot make the necessary changes in food intake. An understanding of what motivates people to donate blood could lead to a stable blood procurement system.

Information gained from research in the past 25 years has begun to move medicine away from care of the crises of illness toward the maintenance of health. In the former situation, the ill patient played little role, but in the present situation, his motivation to help himself is the vital, and often lacking, ingredient. If this National Program is to be successful, much new information will be needed concerning the mechanisms of motivation for self-help or self-destruction.

IV. EDUCATION, CONTROL AND PREVENTION

The Council believes that, in response to Section 414 of the Act, the National Heart and Lung Institute should implement a program of education for control and prevention of heart, blood vessel, lung and blood diseases.

EDUCATION

In the area of public and professional education, the Act provides particular opportunities for progress and vigorous efforts should be made. A few examples include research into the best means for continuing public and professional education; provision of information to the Congress, the public and the professional community; and support of the educational efforts of private agencies.

Real practical progress could be made by inclusion of formal mechanisms for education in each National Research and Demonstration Center (see page 30). An organized effort for scientific communication between investigators, centers, the National Heart and Lung Institute and the community should be strongly supported.

Section 413(d) of the Act stipulates that the Director of the National Heart and Lung Institute shall appoint an Assistant Director for Health Information Programs for the purpose of providing the public and the health professions with health information concerning heart, blood vessel, and lung diseases. In the wording of the Act, blood diseases and blood resources are omitted.

The Assistant Director should stimulate a program of research on improving the effectiveness of education in heart, blood vessel, lung and blood diseases. He should also be responsible for coordinating educational and informational programs of the National Heart and Lung Institute with voluntary health agencies such as the American Heart Association, American Lung Association, American College of Chest Physicians, American College of Cardiology.

The Council suggests that the Assistant Director involve the appropriate voluntary health agencies in these efforts because of their longstanding interest and ongoing programs of public education and information.

Furthermore, the Assistant Director's activities should be legally expanded to include education in regard to blood diseases and blood resources.

A major effort must be made to formulate suitable programs for encouraging the public to develop habits that may be of benefit in preventing the development or progression of heart, blood vessel, lung and blood diseases. The public and professional mass education techniques now used to alter health practices are notoriously ineffective. They should be replaced by an effective program of education regarding the pre-

vention of disease and the importance of early detection and treatment. Sociologists, behavioral scientists and psychologists should be asked to assist in developing and conducting studies that focus on motivation and methodology.

CONTROL AND PREVENTION

The Council believes that a limited number of demonstration projects should be developed to:

- Test methods for the education of the public and professional community;
- Demonstrate the feasibility and advantages of community and regional care systems for specific diseases;
- Demonstrate the clinical applicability of the results of research;
- Develop effective prototype community efforts for improved detection, diagnosis, treatment and follow-up of persons with heart, blood vessel, lung and blood diseases, including training of allied health professionals, many of whom may come from the community; and
- Investigate factors important in public acceptability of research findings.

These programs should have a primary research objective, should be time-limited, should provide only those health care services necessary to the project and should be reported in media designed for clinicians, health workers and the public. In all instances, there should be cooperation with existing health resources so that procedures once generated and demonstrated to be effective can be incorporated into ongoing health programs.

The following are examples of demonstration programs which are already under way or should be started in the near future.

- The early detection of hypertension, treatment by drugs and control of long-term complications is already under way. This involves public education, clinical application of research findings, and provides for further research into the disease process.
- The benefits of very early diagnosis and treatment of congenital heart disease should be demonstrated. This would be based on intensive public and professional education regarding the benefits accruing from very early diagnosis and acceptance of care at a single regional center. The project would also bring increased numbers of early diagnosed infants into prospective studies of clinical management.
- The prenatal diagnosis of hyaline membrane disease should be demonstrated by a regional center. Mothers in whom the diagnosis has been made should deliver in the regional center where all available, specialized, and research-proven techniques for management of the disease can be applied. Mortality of affected infants should be very much reduced by this intensive early care.
- An effective means to control smoking needs to be developed and demonstrated. Despite the widely disseminated knowledge that smoking is implicated in heart, blood vessel and lung diseases, as well as cancer, the use of tobacco in this country is increasing. Overall data for all diseases resulting from smoking indicate that the average smoker shortens his life by approximately four years, while some categories of smokers, such as those who begin at an early age and smoke several packs of cigarettes a day, may shorten their lives by a statistical average of as much as eight years. A program to motivate people to stop smoking would be entirely one of education but one which would require full community support and participation. The Council strongly recommends implementation of such a program in conjunction with other Federal and non-Federal agencies.

When Federal funds are used for demonstration projects, care must be taken to avoid replacing local support. Such projects, by their very nature, are time-limited and Federal support ultimately will be withdrawn. Each project should be designed from the outset to include a critical evaluation of its worth and effectiveness. Each is thus a research project investigating the feasibility of translating research results into reality in the health care system. When this translation is complete, local sources of support will be required for continuation of the program.

INTERAGENCY TECHNICAL COMMITTEE

Section 416 of the Act provides for establishment of an Interagency Technical Committee, with the Director of the National Heart and Lung Institute as Chairman, responsible for coordinating those aspects of Federal programs that deal with heart, blood vessel, lung and blood diseases and blood resources.

Many agencies, public and private, have their own programs of research, education or public information in these areas. Of the Federal agencies, the most important are the National Institutes of Health (NIH), Health Services and Mental Health Administration (HSMHA), Food and Drug Administration (FDA), Veterans Administration (VA), Department of Defense (DOD), National Aeronautics and Space Administration (NASA), Atomic Energy Commission (AEC), Environmental Protection Agency (EPA), Department of Transportation (DOT), Social and Rehabilitation Services (SRS), Social Security Administration (SSA), Department of Agriculture (DA), and National Science Foundation (NSF). All are represented on the Interagency Technical Committee.

For an effective National Program, the Council believes that all appropriate efforts of Federal agencies should be coordinated by a committee with responsibility to:

- **Know the full extent of the effort presently supported by all agencies, and that planned for the future;**
- **Avoid needless, unproductive overlap of effort;**
- **Identify neglected fields that deserve considerable expansion of effort;**
- **Provide the best scientific advice on large cooperative programs before they are approved and launched; and**
- **Assure all agencies rapid access to knowledge developed in all programs. The Council hopes that private agencies will also participate in this national effort to exchange information and coordinate programs.**

The National Heart and Lung Institute should ensure that, through the Interagency Technical Committee and other means, advances resulting from research in heart, blood vessel, lung and blood diseases are incorporated into other national health service programs; for example, emergency services that emphasize cardiac and pulmonary resuscitation should incorporate research advances in electrophysiology and resuscitation.

V. SCIENTISTS AND THEIR SUPPORT

To accommodate the needs for both fundamental and mission-oriented researc!., the National Heart and Lung Institute requires a wide variety of support mechanisms suitable to a wide variety of investigators. Some investigators do their best work alone, others do best when working in small groups; still others are most productive when they have the stimulus that comes from frequent exchange of ideas in a large interdisciplinary center. Some investigators are highly imaginative and generate their own ideas, and some are less innovative but are highly productive in following leads of others or working in collaborative programs with carefully designed protocols. Whatever the system for the support of research, it must both favor the imaginative, innovative investigator and provide for flexibility to explore new leads whenever and however they are identified.

The recent fluctuations in Federal support of research have, by lowering morale, made careers in biomedical science far less attractive than they were some years ago and thus have been costly to a sustained research effort. The assurance of more positions with more stability will do much to attract and keep brilliant and creative scientists in heart and blood vessel, lung and blood research.

RESEARCH PROFESSORSHIPS

The Council acknowledges the considerable stimulus to investigators that comes from close association with medical and graduate students and from observation of patients. But it also believes that the rapid advance of the National Program requires that more senior scientists dedicate 80 to 90 percent of their time to research. Therefore, the Council proposes that stable positions should be made available for senior investigators who wish to devote their main efforts to research on the heart, lungs or blood. Further, long-term national goals will be achieved more quickly if every school of medicine has such a stable position to offer a scientist who can develop a vigorous heart and blood vessel, lung or blood research program.

> The Council recommends, as a very effective means of accomplishing national goals, that the National Heart and Lung Institute should establish a Research Professorship in every medical school in this country. Approximately $10,000,000 a year should be appropriated, and allocated, for this purpose.

The Council envisions this as stable support, through a long-term grant, of a *position* in each school of medicine rather than the support of a specific research project. An established senior investigator would be named by the school but must be acceptable to the National Heart and Lung Institute. During his tenure in the position, he would be freed from all but minor responsibilities of teaching, administration and clinical care.

> The concept of the Career Investigator is one used quite effectively by the American Heart Association (AHA) since 1951. Its philosophical approach toward the support of research has been one of supporting people rather than their projects in the conviction that the decrease and the eventual elimination of cardiovascular disease can best be achieved through a stable, consistent research effort by the most talented and productive minds available. The record of achievement by the recipients of AHA Career Investigator awards bears out the soundness of that philosophy. The AHA has found that the work of Career Investigators is cited more than twice as often in scientific literature as the work of "top candidates" who were nominated for the investigatorship but did not receive it. Further, the AHA Career Investigators, now freed from responsibilities unrelated to their career goals, have attained a level of productivity considerably higher than that before accepting the award. The award has not removed their work from peer review since they must secure much of their research expenses through national competition. In addition, the Career Investigators have an impressive record for teaching students and training young scientists. The Council believes this is a program which should now be greatly expanded with the support of the National Heart and Lung Institute.

The Council strongly urges that a grant be awarded to each medical school in this country to create these positions. Each initial grant would be for a 10-year period, renewable for additional 10-year periods. The grant should include full salary of an established investigator at either the professor or associate professor level. In some schools it may be necessary to support this position at a salary level above the scale of the institution if an investigator of high quality is to be obtained. It is further recommended that the grant should include a full salary for a research fellow and for a technician to work with the investigator; plus $15,000 a year for partial costs of their research. The average amount for each unit in FY 74 would be $75,000 plus an additional amount for indirect cost allowance. Funds should also be made available for initial renovation of space and purchase of equipment if necessary during the first year of a new incumbent. The total funds required would be approximately $10,000,000 a year. The Research Professor, like the Career Investigator of the American Heart Association, would be expected to compete for additional research support, as needed, through other mechanisms, and these generally require competitive scientific review.

Each medical school would thus have assurance of stable funds for a senior research position so that it could actively recruit a scientist to fill it (although funds would not be released until a school has nominated an acceptable candidate).

> Institutions should have the widest possible latitude in selecting a nominee. He could already be a member of the faculty of that school or could be recruited from elsewhere; he could hold an M.D., Ph.D., or other appropriate post-doctoral degree. He could work in a basic science or clinical department or both. Although his field of research at the time of his appointment would be in the heart and blood vessel, lung and blood area, broadly considered, he would be free to change direction within the field. The Research Professor would commit all of his effort to research except for a small amount to be spent in related teaching or training.
>
> A candidate accepted for a position of Research Professor would hold the post only as long as he continued to devote his main energies to research. If, for any reason, the recipient left the institution, he could not transfer the award to his new school. If he accepted responsibilities that decreased his commitment to research, he would no longer be eligible for the award. If, at the end of the grant period, a peer group found him to be unproductive, he would not be eligible for another term. Under these circumstances, the school would be required to nominate a new candidate. The funds would not be available to the school when the position was not filled, but would be released upon acceptance of a new candidate by the National Heart and Lung Institute.
>
> This program, designed to provide long-term stable support, would require a long-term commitment on the part of the National Heart and Lung Institute. But it would also require a considerable commitment on the part of the medical school, which would be expected to provide space and assurance of stability of appointment for the recipient.

There are a number of advantages of making such an award to each school. It would at once be a national

program, since the awards would be geographically distributed throughout the country with each school having one such award. Further, the promise of stable and adequate support for a senior research position would help a smaller school with limited resources to attract a competent investigator who would then become the nucleus there for an expanded research effort on heart, lungs, or blood. This could well be a means of upgrading schools which at present have difficulty in competing successfully for National Heart and Lung Institute or other research support. At the same time, the program should have a beneficial effect on teaching medical students and training interns and residents in areas related to the heart and blood vessel, lung and blood field.

PROFESSORIAL RESEARCH GROUPS

The Research Professorship described above would assure support of a minimal research unit in each school for an individual scientist who wishes to devote his main energies to research. But to achieve the goal of conquering the diseases of the heart, lungs and blood, many more talented, imaginative men and women must be induced to enter and stay in careers in research related to these diseases. Universities, hospitals and private research institutes do not have the financial resources to pay the salaries of these additional research scientists and their support can come only from the Federal Government.

As a means of expanding the number of stable positions for creative scientists without draining the now-limited financial resources of universities and other private organizations, the Council recommends that $15,000,000 a year be allocated to the National Heart and Lung Institute for the support of Professorial Research Groups, each consisting of several competent investigators. Fifty such units should be established at an average cost of $300,000 per year; 40 should study disorders of the heart and blood vessels and/or lungs and 10, disorders of the blood.

Professorial Groups have been supported for some years by the Medical Research Council of the United Kingdom as a means of attracting talented scientists into careers in medical research and of stimulating or expanding research in certain selected fields of national need; the United Kingdom program has been a very successful one.

The Council proposes that a grant to support a group usually should include full salary for a professor (who would be the director of the unit and would be assured of long-term support from the grant) and three associate professors or assistant professors. The grant should also include salaries for three technicians and approximately $50,000 a year for partial research expenses of the laboratory. With the addition of appropriate indirect costs and allowance for a degree of flexibility to compensate for local conditions, each unit would cost approximately $300,000 per year. Groups would be expected to obtain additional support as needed through other mechanisms. Grants for Professorial Groups would not be reserved for each school of medicine, but would be awarded on a competitive basis and only after competitive scientific review. They would be awarded for seven years, and should be renewable for seven-year periods.

The director of the group may be associated with a university, its medical schools or hospitals or a non-profit research institute; he may hold the M.D., Ph.D. or other appropriate postdoctoral degree. He may be a member of a basic science or clinical department or of both and his application may request support for either basic or clinical research or both. Important considerations in its review would be the excellence of the proposed research program, its relation to the solution of heart and blood vessel, lung or blood problems, its long-term nature and the commitment of the group to devote all of its time to research for the period of the grant, except for a small amount that may be spent in related teaching and consulting activities.

A grant for a Professorial Research Group differs from one for a Research Professorship in that the former is an award to a small group of scientists who propose a specific research program and the latter is an award to a school of medicine to support a research professor. The grants are similar in that each has a goal to attract and keep competent scientists in full-time research by providing long-term and full support of professorial salaries.

RESEARCH CAREER DEVELOPMENT AWARDS AND SPECIAL RESEARCH FELLOWSHIPS

Phasing out the current programs through which the National Heart and Lung Institute pays the salaries of 200 established scientists who now devote almost full-time to research important to the National Program could diminish the national research resources by 200 scientists.

The Council urges that the Administration find an acceptable way of restoring these stipends and permitting important research to continue.

EDUCATION OF YOUNG SCIENTISTS

The Council believes that a critical need *now* for long-term success of the National Program (i.e., prevention and elimination of diseases of the heart, blood vessels, lung and blood) is recruitment and training of young scientists.

The Council sees no way to attain the long-term goal without the means to recruit talented young men and women and to provide excellent training for their research careers. These scientists-in-training (now called pre- or postdoctoral Research Fellows or Trainees) are absolutely essential to the Program for several reasons:

- They are needed to replace present investigators who die, retire or change careers.

- In certain long-neglected areas (e.g., lung disease), there is such a shortage of scientific personnel and scientist-teachers that a national program in research and education must limp along until a large number of young scientists is recruited and trained. The Lung Diseases Panel has emphasized that a diversity of scientists is needed—not only medically trained scientists but also basic scientists in the areas of physiology, biochemistry, biophysics, genetics, immunology and epidemiology.

- Research Fellows and Trainees are required for the actual conduct of much of the National Heart and Lung Institute research now in progress—research supported by research project grants, program project grants and specialized centers of research.

- Although less readily understood by laymen, an equally important reason for support of Research Fellows and Trainees is the stimulus provided to senior scientists by the merciless questioning of inquisitive, critical, young men and women who have different backgrounds and different scientific prejudices than their mentors. New blood brings new questions and new ideas; turnover of Research Fellows and Trainees every two to three years represents an inexpensive and effective way to maintain and increase scientific productivity of senior staff.

- An effective way of establishing communication and cross-fertilization among research groups working in different parts of the country is the training in one institution of postdoctoral Fellows who subsequently will work in another.

The Council strongly believes that the education of young medical scientists is clearly a national responsibility.

- Young scientists are a valuable national resource and their development is a national obligation since their work benefits all of our people in all 50 states. No one would ever consider the possibility that each state and each community should make its own medical discoveries and reserve these for its own residents. New methods of treatment discovered in Mississippi are applicable at once to California; new diagnostic methods devised in Massachusetts are applicable immediately to Alaska.

- States and regions vary greatly in their ability to support medical research and training. National support is needed to prevent discrimination because of economic, geographic, minority or other factors.

- Unlike medical practitioners who usually practice in the state where they have received their medical or postgraduate education, medical scientists who are trained in a limited number of centers of excellence more often spend their research and teaching careers in another of our 105 medical schools in another of our 50 states.

The Council unanimously and strongly urges that funds be allocated to the National Heart and Lung Institute to train young men and women for research careers.

The Council has considered the advantages and disadvantages of several mechanisms that have been proposed. Four alternatives are identified.

- *Loans for Trainees.* This mechanism has the advantage of little or no cost to the Federal Government but the disadvantage that it cannot possibly meet the special needs of the National Heart and Lung Institute. It is unrealistic to believe that the most innovative and creative young men and women will also be the most idealistic who will elect to accumulate an additional debt of $20,000 to $30,000 to obtain two to three years of research training (after a long period of financing their college and professional education) when the alternative is to *earn* over the same period $24,000 to $36,000 as hospital residents. A loan system will surely result in exclusion of practically all economically disadvantaged people from advancing their careers in medical science at a time when the Federal Government has a policy of affirmative action.

  There is no reason to believe that those who *do* have the independent financial means to obtain training in science will favor careers in cancer or heart, blood vessel, lung and blood research at a time when the conquest of cancer and heart disease has been assigned top national priority. To assure success for the Program, financial incentives must be added for training young scientists.

- *Stipends for Research Fellows and Trainees.* This mechanism would require allocation of sufficient funds to the National Heart and Lung Institute to award Traineeships or Fellowships, the number in various areas of research to be determined annually by the National Heart and Lung Institute with the objective of meeting the needs of the National Program. Awards would be made after competitive review to individual applicants on the basis of their past record, promise for future achievement and acceptability by an institution and scientists judged by the National Heart and Lung Institute to have outstanding capability for research training.

  Important advantages of the program are that it provides diversity of training opportunities and that the presence of Research Fellows in the diverse research laboratories acts as a catalyst to increase the quality of research generated in the laboratories. A disadvantage is that broad scientific training is not a required part of the program.

- *Research Training Program.* The Council at its March 1972 meeting agreed with the Administration that important modifications were needed in its Graduate Training Programs. The Council decided that the National Heart and Lung Institute needs a program designed to train those research scientists required to achieve the goals of its National Program and that the number and types of Research Trainees should be reviewed periodically.

  Such a program has the disadvantage of costing more in that it requires support for *programs* (faculty and supporting staff) as well as for *stipends*. It has the advantage that the training program itself is subject to competitive scientific review to ensure that Trainees receive total scientific education and training needed to equip them best for future research careers.

- *Salaries for Scientific Staff.* In the event that none of these programs is funded adequately, the Council has no alternative but to request additional research funds to pay for scientific staff to replace those lost by not paying Trainee stipends. It has not been generally recognized that each pre- or postdoctoral Research Trainee or Fellow spends at least 30 to 40 hours per week in research ("on the job") training under the supervision of a senior scientist. There are now 995 full-time Fellows or Trainees and 350 part-time Trainees supported by National Heart and Lung Institute Research Fellowships and Graduate Training Grants; of these, 675 are full-time Trainees in research and 670 are part-time. Elimination of these reduces by 675 the number of full-time scientists and by 670 the number of part-time scientists now engaged in heart and blood vessel, lung, and blood research. It is essential to replace these with research assistants to maintain the present level of research activity in the laboratories where Trainees now work.

In considering mechanisms for funding, Congress should remember that the last mechanism noted above will increase indirect costs from 8 percent on each stipend (allowed on Training Grants) to an average of approximately 50 percent on each salary (allowed on Research Grants).

EFFECTIVE UTILIZATION OF SCIENTIFIC MANPOWER

Although the Council is justifiably concerned about production of scientific personnel for research programs in future generations, it is equally concerned with full and effective utilization of the presently trained scientific manpower. It is clear from the number of research grant applications received by the National Heart and Lung Institute each year, as well as from the number of these applications that are considered to be meritorious but cannot be funded, that there is a large body of scientific manpower now available to perform more heart and blood vessel, lung and blood research than can now be funded. Many of the proposals already made in this Council report are aimed at full utilization of this manpower while also achieving the goals of the National Program. However, most of the mechanisms that have been innovated in the last few years for increasing the rate and quality of research productivity have favored support of larger programs of research, all of which have a tendency to increase the support of research groups in medical schools and other medical centers that are already among the better supported. There is justifiable concern on the part of many of our smaller institutions that the present trend can redistribute research manpower in such a way that it leads to weakening of research in many of our less affluent medical schools and centers. Furthermore, because the less affluent schools train a significant proportion of the doctors of our nation, the presence of good research programs in these schools will have double pay-off: first, for the research results themselves and, second, for their value in enhancing the quality and quantity of the training programs in all sectors of our nation.

The Council recommends that a committee be formed, composed at least three-fourths of persons from smaller institutions, that will report annually to the Council on ways and means of increasing the participation of the smaller and less affluent medical schools and certain other medical institutions in the national heart, blood vessel, lung, and blood research effort.

The Council further recommends that such institutions be offered assistance in the development of their programs.

Medical schools and other institutions whose ratio of Federal to local support is low should have the privilege of requesting an annual visit from an ad hoc committee chosen and detailed by the National Heart and Lung Institute. The purpose of the visit would be to help the institution select from among its personnel those who are worthy of research support and to establish a plan and a budget for funding their research. The committee shall then submit this for consideration and scientific review by a consultant panel responsible to the National Heart and Lung Institute. This panel, in turn, shall recommend a budget for support of specific research projects in such institutions. Projects thus supported, however, must have priority ratings that would be fundable in competition with other research and program project grants supported by the National Heart and Lung Institute.

VI. FISCAL MECHANISMS: GRANTS, CENTERS, CONTRACTS

Many fiscal mechanisms are available for implementation of a National Program. The ways in which they are used must be responsive to the goals, and must permit a planned and systematic exploration of promising avenues and the rational assignment of priorities. At the same time, a degree of flexibility must be maintained and the mechanisms of support must foster creative innovation and allow for new and unplanned breakthroughs. No one fiscal mechanism will achieve these goals. In this section, the Council reviews the present methods of support and makes specific recommendations.

RESEARCH AND PROGRAM PROJECT GRANTS

The Council strongly endorses the current research grant programs that support investigators who generate their own ideas and can pursue these ideas independently; their research may be basic or clinical.

The Council gives its highest priority to support of independent research that may lead to more basic knowledge in all areas related to diseases of the heart, blood vessels, lungs and blood, even though the connection may not be immediately apparent. Increased funding for research projects and program projects initiated by investigators is essential to this effort.

The FY 73 National Heart and Lung Institute budget of approximately $100,000,000 for such grants should be increased by 25 percent in FY 74, and by an additional 25 percent in each of FY 75 and 76. In FY 77 and beyond, the level of support of these programs should be maintained in terms of actual buying power of the dollar. The increases are needed for the following reasons:

- The actual amount of research "purchased" with National Heart and Lung Institute funds has *decreased* year by year as salaries of scientists and their supporting staffs, costs of supplies, services and equipment, indirect costs of research and fringe benefits have risen far beyond the increase in funds allocated for research project and program project grants;
- Many approved research projects that may be important to heart, blood vessel, lung and blood research have not been funded; and
- The National Program requires an influx of young and senior scientists not now working on National Heart and Lung Institute programs.

When a research project or program project receives a priority that places it within the top 25 percent of grants approved in competitive scientific review, an award of up to seven years should be made (unless inappropriate due to the nature of the research project) to provide stability of support. Similar long-term awards should be made whenever the nature of approved research requires a long period to obtain essential data.

SPECIALIZED CENTERS OF RESEARCH (SCOR's)

The National Heart and Lung Institute recently initiated a program of support of Specialized Centers of Research to speed the development of new knowledge essential for improved diagnosis, treatment and prevention of specific diseases by focusing resources, facilities and manpower on particular problems. The diseases and the specific problems for investigation in a SCOR are first identified by the National Heart and Lung Institute. Applications are then invited and reviewed. Funding is by the grant mechanism. The effort in most SCORs is a multifaceted one and includes both basic and clinical research. SCORs have been activated in arteriosclerosis, hypertension, thrombosis and pulmonary diseases.

SCOR activities are coordinated by the National Heart and Lung Institute staff. Active cooperation among Centers is expected, and in fact required, to speed the dissemination of new knowledge. The Council endorses the concept of the Specialized Centers of Research as an effective means of mounting a National Program in certain disease categories.

> **The Council recommends that additional Specialized Centers be supported for study of other clinical problems (such as heart failure, and diseases of the heart, lungs and blood in the newborn) and for improving national resources (such as blood banking) when there is a reasonable chance that the initiation of a SCOR will result in more rapid acquisition of specialized knowledge and its application.**

NATIONAL RESEARCH AND DEMONSTRATION CENTERS

Section 415 of the Act states that the Director of the National Heart and Lung Institute may establish centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention and treatment methods (including methods of providing emergency medical services) in heart, blood vessel, lung and blood diseases. Such centers have yet to be established. There could be as many as 15 for heart, blood vessel and blood diseases and 15 for lung diseases.

Centers should not necessarily attempt to encompass all the provisions of the Act. For the purpose of the National Program, the emphasis should be on the acquisition of new knowledge. To this end, they may be centers for basic research utilizing many scientific disciplines but devoted to the study of one area (e.g., pathogenesis of atherosclerosis or thrombosis, biology of the normal lung). Or, they may combine both basic and clinical studies, serving as an important mechanism for bridging the gulf between fundamental research and application of results to patient care. Although centers of the latter type may be concerned with research into improved methods of diagnosis and treatment, they would carry on patient care only insofar as it relates to their specific research efforts. After improved methods of diagnosis and care are developed and demonstrated by such centers, the Interagency Technical Committee would be an appropriate mechanism through which broad clinical applications could be planned.

The idea of the interdisciplinary, multidepartmental, comprehensive center is an important one in planning how best to fulfill the requirements of the Act. Such centers provide a critical mass of scientists in many disciplines. This facilitates sharing of ideas and knowledge, hastens the exploration of new ideas, provides for critical evaluation of ongoing work and creates an ideal setting for training future biomedical scientists.

In addition to engaging in broadly based and intensive scientific endeavors, a center should have a keen sense of responsibility in regard to professional and public education and information and of commitment to the overall purpose of the National Program. An education and information program, insofar as possible, should be an integral part of each center's activities. The medical profession should know of the center's scientific activities and the new knowledge these generate. The public should be kept informed on matters relating to health and control of heart, blood vessel, lung and blood diseases and the center's contributions to these areas of knowledge.

> **The Council agrees that establishment of such comprehensive centers would be an appropriate mechanism to meet the goals of the National Program.**

Before activating any centers, however, the National Heart and Lung Institute should carefully consider such matters as optimal size and location; the initial number to be established; establishment of additional centers according to changing needs of the National Program; avoidance of a rigid, organizational plan to which each center must conform; a mechanism for review and evaluation of overall achievements, strengths and weaknesses; a mechanism for phasing out unsuccessful centers; the effect on other programs of

the National Heart and Lung Institute caused by allocating large sums of money to centers; and the effect on national distribution of scientific manpower that might be caused by establishing centers.

The Council believes that administrative arrangements should be determined individually according to each center's relationship with its parent organization and its unique research support needs.

CONTRACT-SUPPORTED RESEARCH AND DEVELOPMENT

Until recently, the National Heart and Lung Institute has supported research largely by grants awarded (after competitive scientific review) to scientists to work on problems *they* judge to be important (investigator-initiated grants), whether in basic or clinical fields. Recognition that sole dependence on investigator-initiated programs may result in neglect or under-emphasis of some scientific areas has led to the use of contracts to support research identified as essential to national needs by Institute staff, or its appointed consultants, committees, task forces or commissions.

In addition to work on important problems not being studied sufficiently under the grant mechanism, the Institute now supports by contracts work on those problems that require large-scale cooperative efforts, collaboration of many research units and expert advice on design of experiments and evaluation of data. The latter include clinical trials in detection and management of hypertension; studies on the importance of risk factors in coronary heart disease; nationwide studies on blood lipids; intensive study of myocardial infarction in patients in special research units; and clinical trials of therapy for sickle cell disease. Contracts also finance special needs such as management of blood resources, development and testing of medical and surgical devices (including devices to assist or replace the failing heart and lungs), and provision for special surveys of research manpower needs.

The Council believes that the contract mechanism is essential for support of important research that would otherwise not be attempted. A careful balance must be struck, however, so that the future growth of the contract programs will not be at the expense of investigator-initiated, grant-supported research. The Council agrees that national planning *is* essential to mount a truly balanced program but believes that planning by a few highly competent individuals (either the permanent staff of the National Heart and Lung Institute or extramural scientists appointed to task forces or commissions) should supplement, but not replace, individual thinking by perhaps thousands. When the way ahead is not clear and a science base is lacking for a successful *directed* research effort, what is needed is an abundance of original ideas; these are most likely to come unpredictably from the imagination and intuition of individual scientists working in their laboratories, and less likely to come from administrators or their committees. There is a considerable risk for the future of the program in giving full authority for decisions about fruitful areas of scientific investigation to a relatively small group of either administrators or scientists. However, wise counsel at the national level can lead to acceleration of some important research programs when the needed research can be clearly predicted in orderly progression, and it can often lead to projects that secure valuable information difficult or impossible to obtain through the initiative of individuals.

For these reasons, the Council recommends that as the use of contracts for support of research increases:

- This growth shall not be at the expense of the support of basic or mission-oriented research initiated by individual investigators;
- The areas of research to be supported by contract should be approved by the Council in advance;
- The scientific merit of research to be supported by contracts should be evaluated by consultant review groups before contracts are issued;
- Regular Council review should be required for contracts as well as for grants.

The Council believes the contract should be considered a means for achieving a scientific goal rather than as an end in itself. To this end, it is recommended that the chief Federal officer responsible for contracts should be a member of the professional staff of the Institute and that the fiscal and legal administrators be advisory to him.

The Council also recommends that the National Heart and Lung Institute should make every effort to permit freedom in the conduct of contracted research if such freedom does not defeat the purpose of the contract.

For the contract mechanism to be truly effective, furthermore, it should provide greater stability of support than is now possible with an award limited to one year and the uncertainty of renewal year by year; the duration of the contract should be appropriate to the nature of the work. Evaluation of the contract program should be part of the annual review by the Council and its report to Congress.

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VII. CONSTRUCTION

A lack of modern facilities for basic and applied research limits the advance of heart, blood vessel, lung and blood disease research in this country and, consequently, threatens the success of the National Program.

To mount a successful National Program against diseases of the heart, lungs and blood, the Council recommends that $60,000,000 be obligated for this purpose in FY 74 (thus enabling construction of research facilities to be started without delay) and $30,000,000 in each of FY 75 and FY 76.

The basic sum in all years is for increasing the research capabilities of scientists working in existing programs of the National Heart and Lung Institute. The additional sum in FY 74 is to develop National Research and Demonstration Centers.

Because the results of research benefit the entire nation, recipient institutions should not be required to provide matching funds. National interests are best served by making construction funds available to those scientists and institutions that, given additional facilities, can make the greatest contibution to the National Program rather than to those whose scientific contribution may be less but whose institutions have non-Federal funds on hand to match Federal funds. The availability of complete Federal funding for construction would permit financially troubled schools to apply and to increase their research effort toward achieving national goals and would lessen redistribution of scientists from poor to rich schools.

Funds in a research grant may now be spent for alteration and renovation of existing research facilities. The present limit is $75,000 or 25 percent of the amount of the grant, whichever is less. The Council recommends increasing the upper limit to $250,000.

VIII. BUDGET

1. FIVE YEAR BUDGET PROJECTION

The Council's projections for annual program budgets for the next five fiscal years (together with historical data from fiscal year 1972 and 1973) are presented in the Table on the following pages.

2. MULTIYEAR FUNDING

Tentative plans for any major new program, such as new Specialized Centers of Research or National Research and Demonstration Centers or new clinical trials, can be developed in advance, but requests for applications or proposals must await appropriation and allocation of funds. When these come late in a fiscal year, there is pressure on the National Heart and Lung Institute staff to complete and promptly announce plans to the community, and pressure on potential applicants to develop and submit proposals on short notice. This may limit applicants to a few institutions whose resources are already available and whose organization is already established, and exclude other institutions that might qualify, given more time to plan and organize. These problems are serious ones in that the excluded institutions might well develop the best programs. The problems can be avoided if the National Heart and Lung Institute is permitted to retain the funds intended for specific purposes beyond the fiscal year in which such funds are appropriated.

The need for more preparation time is particularly important for Center programs which require advice of extramural experts and consultations with the Council; a large commitment by the applicant institution of personnel, facilities and resources; interdepartmental cooperation and collaboration; and a good plan for internal management and administration. The need to retain funds is equally important in programs, such as clinical trials, that require a tool-up, phase-in time that may not be entirely predictable. Multiyear funding would also allow consultant review groups more time for objective evaluation and rating of proposals.

> The Council recommends that funds for specifically identified programs should remain available to the National Heart and Lung Institute, for the purpose originally intended, until the end of the fiscal year subsequent to the one in which such funds were appropriated so that programs can be implemented on the basis of carefully developed plans, even though this may not be possible within the fiscal year of appropriation.

3. NEEDS FOR STAFF AND FACILITIES, NATIONAL HEART AND LUNG INSTITUTE

The Council's recommendations for increasing many existing programs of the National Heart and Lung Institute and for creating new programs, as well as the

NATIONAL HEART AND LUNG INSTITUTE
FY 1972 (OBLIGATED): FY 1973 -- FY 1978
(DOLLARS IN THOUSANDS)

Program Activities	FY 1972 (obligated)	FY 1973 (estimated)	FY 1974 (estimated)	FY 1975 (estimated)	FY 1976 (estimated)	FY 1977 (estimated)	FY 1978 (estimated)
Research Projects and Program Projects	$102,835	$108,821	$141,113	$176,391	$220,488	$231,500	$243,100
Arteriosclerosis	(26,458)						
Cardiac Diseases	(22,106)						
Hypertension and Renal Diseases	(14,005)						
Pulmonary Diseases	(7,617)						
Thrombosis and Hemorrhagic Diseases	(12,117)						
Sickle Cell Disease	(5,581)	(8,000)	(9,500)				
Multidisciplinary	(14,951)						
Special Projects							
1. General Research Support Grants	8,325	8,149	---	---	---	---	---
2. Heart Cooperative Drug Study	3,514	4,900	4,900	500	---	---	---
3. Specialized Centers of Research	20,584	22,700	30,000	35,000	40,000	42,000	45,000
Arteriosclerosis	(9,515)						
Pulmonary	(6,467)						
Hypertension	(2,496)						
Thrombosis	(2,106)						
Other (see text)	---						
4. Control Programs*	---	---	5,000	15,000	30,000	31,800	33,700
5. Research Professor Grants	---	---	10,000	10,600	11,300	12,000	12,700
6. Young Scientist Education**	---	---	2,000	10,000	12,000	12,700	13,000
7. Professorial Group Grants	---	---	15,000	15,900	16,900	18,000	19,000
8. National Research and Demonstration Centers	---	---	24,000	36,000	48,000	51,000	54,000
9. Construction	---		60,000	30,000	30,000	0	0
Subtotal, Research Grants	135,258	144,570	292,013	329,391	408,688	399,000	420,500
Fellowships and Training Grants:	24,905	22,000	17,139	12,000	6,000	---	---
Laboratory and clinical research	18,259	18,741	20,376	22,000	24,000	25,400	27,000

R&D Contracts:							
Heart and vascular:							
Myocardial Infarction (MIRU, SDS, and anti-arrhythmic drugs)	8,027	9,980	10,500	13,000	14,000		
Lipid metabolism	5,485	8,378	10,400	11,000	11,700		
Hypertension clinical trials	3,971	6,100	7,400	8,500	9,000		
Heart cooperative drug study	424	450	500	---	---		
Multi-risk factor trials	3,268	7,240	10,000	12,000	12,000		
Education programs-hypertension*	---	---	2,000	3,000	4,000		
Other clinical applications	1,108	1,307	750	1,000	5,000		
Subtotal, Heart and vascular	22,283	33,455	41,550	48,500	55,700	59,000	62,600
Respiratory diseases	1,585	2,330	2,885	8,000	10,000	10,600	11,200
Technological applications	10,572	9,600	12,500	14,000	15,000	15,900	16,900
Blood diseases and resources:							
National blood resources	5,504	5,500	8,000	12,000	15,000		
Thrombosis clinical trials	---	---	5,000	5,000	6,000		
Sickle cell: research	2,326	3,500	3,700	4,000	4,500		
clinics, HSMHA*	1,975	2,000	3,800	4,000	3,000	2,000	1,000
Subtotal, Blood diseases and resources	9,805	11,000	20,500	25,000	28,500	29,000	29,700
Other:							
National plan	---	1,000	600	1,000	1,000		
Miscellaneous	354	884	892	1,000	1,000		
Animal models	---	---	1,900	2,000	3,000		
Subtotal, Other	354	1,884	3,392	4,000	5,000	5,300	5,600
Total, R&D Contracts	44,599	58,269	80,827	99,500	114,200	119,800	126,000
Biometry and Epidemiology	1,536	1,700	1,791	1,900	2,000	2,100	2,300
Research Management & Program Services***	8,016	10,000	10,000	12,000	14,000	15,000	16,000
Total	232,573	255,280	422,146	476,791	568,888	561,300	591,800

*Planned under the authority of Section 414 of the Act.

**In the event these funds are not made available, Council recommends the addition of 1.5 times the amounts shown on this line to the amounts for research grants.

***Includes the Office of the Director of the Institute and the scientific administration of grants and contracts.

added responsibilities authorized by the National Heart, Blood Vessel, Lung, and Blood Act of 1972, cannot be carried out without a considerable increase in budget and space for the Institute's Research Management and Program Services. There is urgent need for additional, highly qualified *professional* staff and expert consultants to maintain a high level of competence for program planning and evaluation, for critical scientific analysis of programs, for identification of both neglected and overworked areas, and for coordination of national efforts directed toward early diagnosis, treatment and prevention of heart, blood vessel, lung and blood diseases.

Because the present professional staff of the National Heart and Lung Institute is greatly overextended, the increment in professional staff must be greater than that required simply for new program management if maximum advantage is to be gained from appropriated funds. An indication of the magnitude of the staffing problem is that in the last decade, from 1963 to 1973, the obligations of the National Heart and Lung Institute have increased by 93 percent (from $120 million to $232 million) while the total staff of the Institute has actually *decreased* by 1.3 percent (from 673 to 664).

Several immediate needs present themselves. New responsibilities have been added for lung diseases, blood diseases including sickle cell disease, control programs and the establishment of National Research and Demonstration Centers. Other new demands are created by the expanded activities of the Council and the U.S.-U.S.S.R. Cooperative Health Agreement. Immediate increase in staff is required in each of these areas.

The Council's National Program recommends expenditure increase from $255,280,000 in FY 73 to $422,146,000 in FY 74, an increase of 65 percent. If this budget recommendation is followed, the staff responsible for all extramural programs will have to be increased appropriately to plan and oversee the increase in expenditures. The detailed justification of specific positions will have to be prepared by the Institute. The Council confirms that under-administration can be as wasteful as over-administration.

Similarly the Council calls for an increase in expenditures of 45 percent between 1974 and 1978. An increase in staff certainly will be required to handle this responsibility.

IX. NATIONAL PROGRAM REVIEW AND EVALUATION

ANNUAL REVIEW OF PROGRAMS AND PRIORITIES

The Council is required by the Act to submit a report to the Congress in January of each year on the progress of the National Program toward its objectives. The Council is also required to assist the Director of the National Heart and Lung Institute in preparing an annual report on the five-year plan with annual extensions of the plan. The Council holds these functions to be very important for the success of the plan because the National Program must be flexible and must respond to scientific opportunities and exploit new leads. Therefore, it has set up a schedule for overall review of each of the major programs on which it advises.

- In September of each year, research grant, program project, Specialized Center for Research, contract and other programs will be reviewed with the Director and staff of the National Heart and Lung Institute. Prior to the September Council meeting, hearings may be conducted to reevaluate priorities in each disease area. This will give the Council opportunity to respond to national needs and to take advantage of recent scientific advances. The Council will suggest changes, deletions and new emphases in the National Program priority recommendations.

After the Council discussion at the September meeting, the required report will be written by a subcommittee according to an approved format. Further Council review will be in November or December at which time the report will be forwarded, together with budget, staff and legislative recommendations, to the President and Congress.

In developing its report, the Council will pay particular attention to the effect on the National Program of the provisions of Section 419B of the Act which allocate 15 percent of the National Heart and Lung Institute appropriations to the lung and blood fields respectively.

The Council believes that the experts or consultants authorized by Section 413 (c)(1) of the Act could provide in-depth analysis of the various programs for use in program evaluation, both by the Institute and the Council.

Periodic review every few years by an ad hoc group, separate from the Council, should be considered. Such a group would analyze the Program and recommend improvements in its operations.

PEER REVIEW OF PROPOSALS FOR GRANTS, CENTERS AND CONTRACTS

The system of peer review of research proposals by knowledgeable experts, followed by review by the

Councils, has been one of the most successful undertakings of the National Institutes of Health, and has assured high quality and productivity of the total research effort.

The Council strongly advises that the peer review system, including Council review, should be extended to all parts of the program of the National Heart and Lung Institute.

The Council believes that the peer review system has been as effective for program projects and specialized centers of research as it has been for individual research grants. Before awards are made for National Research and Demonstration Centers for heart, blood vessel, lung and blood diseases, it is important that the same careful review of all scientific proposals be carried out by appropriate experts just as for other types of research effort. The Council believes that, because of the size of these Centers, multiple peer review mechanisms will need to be utilized, including site visits, special and ad hoc review groups, and, when needed for certain individual projects within the Center, referral to study sections.

The Council believes that peer review of contract awards should be as similar as possible to review of research grants. This would entail review by the Council of individual proposals and recommendations of initial review groups.

A special section within the Institute, separate from the ongoing program branches, should be responsible for appointments to peer review groups of the National Heart and Lung Institute.

To assure adequate Council review of proposals in all areas—heart, blood vessel, lung and blood diseases—balance must be maintained in the areas of expertise represented by the scientific members of the Council.

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APRIL 6, 1973

NATIONAL HEART AND LUNG INSTITUTE/NATIONAL INSTITUTES OF HEALTH
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I. INTRODUCTION

On September 19, 1972 the President signed the National Heart, Blood Vessel, Lung and Blood Act of 1972 (Public Law 92-423). This Act recognizes the human, social, and economic impact of cardiovascular, respiratory and blood diseases, and blood resources, and establishes a greater national commitment to them.

The Act requires the National Heart and Lung Institute to formulate and submit a coordinated plan for a Heart, Blood Vessel, Lung and Blood Program. To assist in the formulation of this Plan, four Panels were established to deal with: Heart and Blood Vessel Diseases, Lung Diseases, Blood Diseases and Blood Resources. Within these four major areas 28 separate Task Groups, consisting of approximately 250 medical and scientific advisers, were established. Within the past six months, this group of biomedical authorities has engaged in a concerted, nationwide effort to assess our current understanding of these problems and to identify new opportunities for present and future application. Their assessments, conclusions, and recommendations are contained in four separate Panel Reports.

Certain common elements and interrelationships are clearly discernible within the four Panels. All have noted, for example, the need for studies to evaluate new therapies, the desirability of developing simple and widely applicable techniques for early diagnosis that are both safe and noninvasive, the usefulness of animal models of human diseases, and the importance of defining the fundamental causes of disease so that more rational therapies can be devised.

The individual panel reports focus on four separate areas among which there are many interrelationships. Disordered biological functions seldom involve a single area. As examples, pulmonary embolism begins with thrombosis and involves the lung and its circulation as well as the heart. Effective delivery of oxygen to the tissue depends on the lung, the heart, the amount, type, and functional status of the hemoglobin, and the peripheral circulation.

These biological interrelationships should be translated into specific interdisciplinary approaches, and encouragement should be given to comprehensive heart-lung-blood centers. High priority should be given to the development of projects which use combined clinical and basic science approaches to the various project areas recommended. The epidemiologic studies which are recommended should be based on input from the various clinical and basic science disciplines and be applied to diseases with interdisciplinary dimensions.

Such an approach is desirable not only from the scientific and organizational standpoint, but will tend to conserve resources, space, money and personnel.

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In this report the four Panel Chairmen have highlighted the most urgent and opportune recommendations. To facilitate communication, relatively nontechnical language has been utilized throughout. The Chairmen have not attempted to be all-inclusive. Readers who desire a more comprehensive or more technical description of the findings and recommendations should refer to individual Panel Reports.

In analyzing the scope and variety of the recommendations contained herein, the Panel Chairmen have identified three major categories:

- Those that can be applied *now* for the better prevention, detection, and treatment of disease
- Those that draw upon existing information, but require further testing and evaluation before they can be properly applied
- Those where the current state of knowledge is incomplete and new and basic information must be acquired.

These three categories are linked inextricably, one to the other. The development and broadening of our basic knowledge of health and disease is essential if we are to improve medical care and the quality of life.

The Chairmen wish to emphasize that the control and prevention of disease is a continuing effort that can only be sustained by an ongoing investigative effort. Significant and dramatic advances result from basic research studies.

Often, these advances originate in fields of scientific endeavor not directly related to a particular disease. Therefore, research studies of fundamental processes in health and disease are essential. This requires constant replenishment of able and dedicated medical scientists, as well as updating and maintenance of first-rate research facilities.

The ultimate control of the diseases referred to in this report is, in reality, an international effort and better exchange of information and better coordination would serve to expedite progress and avoid unnecessary duplication.

As an integral part of this effort it will be necessary for scientists, physicians, and the public to engage in a process of continuous and critical review to maintain a high level of effective performance. Such constant and vigorous scrutiny is an expression of social responsibility and will assure objective evaluation of progress, and the updating and revision of plans, the exploitation of new opportunities, and the identification of new directions. It will, in short, help in the development and maintenance of high quality programs that are effective and efficient.

II. HEART, BLOOD VESSEL AND BLOOD DISEASES

2.1 ATHEROSCLEROSIS

Each year in the U.S., one million persons die as a result of cardiovascular disease, and 84 percent of these deaths are attributable to atherosclerosis. Coronary heart disease, stroke, and occlusive disease of the aorta and peripheral vessels are all caused by atherosclerosis; therefore, its prevention and effective treatment would sharply reduce death and disability due to heart and blood vessel disease. International statistics reveal a great variation in the death rates for coronary heart disease. In Sweden, for example, the death rate is 40 percent of that for a similar group in the U.S. This difference indicates that the high death rate due to atherosclerosis in the United States is neither necessary nor inevitable.

Available evidence relates certain risk factors to the progression of atherosclerosis and indicates that it is now appropriate to initiate a major trial of an aggressive intervention program for persons known to be at increased risk and to evaluate objectively its efficacy. These people are at high risk because of a combination of factors as hyperlipidemia, high blood pressure, and smoking. A multifactor intervention program designed to correct these factors and to prevent atherosclerosis and its complications will involve screening, public and professional education, and a system for follow-up and evaluation. Atherosclerosis begins in the young, and, therefore, special attention should be given to the adolescent and young adult, particularly those with a family history of hyperlipidemia. Controlled clinical trials will be required to answer the question: Will modification of risk factors such as diet, hypertension, smoking habits, and sedentary living favorably influence the atherosclerotic process?

In the long run the most rewarding approach will be the development of more effective methods for the prevention of atherosclerosis based upon a better understanding of the mechanisms whereby genetic, environmental, dietary and other factors exert their action. Intensified research efforts should include study of the interactions of the arterial wall and the circulating blood, and the conditions that influence progression and regression of the atherosclerotic lesion.

2.2 HYPERTENSION

Approximately 22 million Americans, or between 10 and 15 percent of the population, have high blood pressure; the prevalence in the black population is probably 30 percent. Hypertension is important because it is a major cause of death and disability *and especially because effective treatment is now available*. High blood pressure has been identified as the most important factor contributing to the development of stroke. It also accelerates the atherosclerotic process in the coronary and peripheral vessels. Control of

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hypertension would therefore reduce the incidence of three major causes of death and disability: stroke, coronary artery disease, and peripheral vascular disease.

It has been demonstrated recently that the control of moderate and severe hypertension by the use of appropriate chemotherapeutic agents (drugs) will reduce the incidence of stroke. This evidence provides the justification for the immediate implementation of a nationwide program to detect and provide, on a continuing basis, effective treatment for all citizens with moderate or severe hypertension. The implementation of this program depends upon the development of a system which utilizes nurses and allied health professionals effectively to deliver the indicated therapy and to motivate the patients to accept it. The beneficial effect of treatment of mild to moderate hypertension on major vascular complications such as stroke and heart attacks has not yet been proven. Therefore, because of its even greater potential importance, this issue should be subjected to clinical trial to define the benefits of long-term treatment.

Antihypertensive drugs provide only a limited solution to the problem of hypertension. Such therapeutic programs require the life-long administration of drugs which often have side effects causing substantial discomfort. For these reasons, the widespread implementation of a chemotherapeutic program for millions of individuals may prove to be impractical. The ultimate solution to the problem will come from identification of the basic underlying disease processes. Areas of investigation which may yield clues to the causes of hypertension are the roles of the renin-angiotensin-aldosterone system, the central and peripheral autonomic nervous systems, other vaso-regulatory hormones, and the role of smooth muscle in the vascular wall in the control of arterial blood pressure and cardiac output. Further study of the kidney is indicated with special attention to intrarenal pressure and flow as signals for the regulation of secretion of renal hormones such as renin.

2.3 THROMBOSIS

Arterial thrombosis does its greatest damage by suddenly completing the arterial narrowing process begun by atherosclerosis. Thus, arterial thrombosis, superimposed on atherosclerosis, is a major contributor to the precipitation of myocardial infarction and stroke, the number one and number three causes of death in the U.S. If arterial thrombosis could be prevented, then the effect of atherosclerosis on life span would be profoundly diminished.

Leg vein thrombosis is the cause of more than 90 percent of pulmonary emboli which are, in turn, responsible for approximately 50,000 deaths annually in this country. Venous thrombosis and pulmonary embolism often occur in the absence of atherosclerosis and are a frequent cause of mortality among patients with underlying cardiac and pulmonary disease, particularly if they are elderly and bedridden. Pulmonary embolism is also the most common, nonsurgical cause of death among adults subjected to major bone and joint surgery. The administration of contraceptive pills likewise may cause an increased incidence of venous thrombosis. Substantial progress has been made in the prevention of certain types of thrombosis. Thus, the benefits of antithrombotic agents in the prevention and management of pulmonary embolism have already been demonstrated in several clinical situations.

Thromboembolism induced by contact of the blood with foreign surfaces remains the major unsolved problem in the development of artificial organs or prostheses for extracorporeal circulation of the blood or for implantation within the heart and blood vessels. Thromboembolism is a major obstacle to advances in medical delivery of care involving artificial heart valves, extracorporeal pulmonary bypass, and cardiac assistance both extracorporeal and intravascular; respiratory assistance through extracorporeal circulation, intravascular catheters, electrodes, and valves for the treatment of hydrocephalus; artificial hearts, artificial blood vessels, vascular sutures, and all other applications in which the blood comes in contact with a nonbiological surface. The present utility of artificial organs depends upon compromises demanded by the lack of materials having long-term compatibility with the blood; there are, at present, no truly nonthrombogenic artificial materials available. Thus, for example, until a nonthrombogenic surface is achieved, no meaningful program for the production of mechanical hearts can be seriously entertained.

Newer antithrombotic compounds are now ready for testing by controlled clinical trials, and these should be launched. Antithrombotic agents generally interfere

with the normal clotting mechanisms and often are associated with undesirable bleeding. A new approach to the prevention of thrombosis in which a concomitant risk of hemorrhage does not occur is needed. To achieve this, the mechanisms whereby fluid blood is converted into a solid plug inside the blood vessel (a thrombus) will require elucidation. Our understanding of the process of thrombus formation will be materially aided by study of the molecular structure and function of the clotting process, and the lining of blood vessels, as well as of the dynamic properties of flowing blood. These results should yield fresh insight into mechanisms of thrombosis which should in turn allow for the development of new methods for prevention and treatment.

2.4 HEART ATTACK: MYOCARDIAL INFARCTION AND ANGINA PECTORIS

Each year over one million Americans have a heart attack (acute myocardial infarction). During this acute attack, 375,000 die. Depending upon their age and health status, between 50 and 70 percent of those patients who have had an acute myocardial infarction survive more than 30 days and are able to return home; many of them, however, are disabled by angina pectoris and congestive heart failure. In still another group the first manifestation of coronary heart disease is angina pectoris, and this is an important cause of disability, especially in men 45 to 65 years of age.

The basic process underlying all forms of coronary heart disease is the narrowing of the coronary arteries by atherosclerosis. When this becomes severe and obstructs the flow of blood, heart muscle supplied by that vessel may be damaged. This condition, in which the blood supply is inadequate to match the needs of the tissue, is known as ischemia. It is the fundamental pathophysiological process responsible for sudden death, myocardial infarction, and angina pectoris. Ischemia is viewed as a critical stage in the evolution of the disease process because at this stage the tissue may return to normal if its blood supply is restored, but if this does not occur the tissue will be irreversibly damaged. Evidence derived from animal experiments suggests that the fate of the tissue in jeopardy can be favorably influenced. For example, reduction in the work of the heart by reducing arterial blood pressure or decreasing the force of contraction, may reduce the size of a myocardial infarction. Another promising approach to the problem of influencing the fate of jeopardized tissue involves alteration of metabolism, and still another approach depends upon the prevention of cell swelling. These therapeutic approaches, developed in the laboratory, should be critically evaluated in patients, utilizing new radioisotopic and biochemical techniques, and other methods for determining infarct size.

Surgical therapy represents yet another approach to the problem of myocardial ischemia in patients with angina pectoris. The value of surgical therapy in bypassing obstructing lesions in coronary arteries in both acute and chronic ischemia must also be critically evaluated.

New and improved methods of minimizing ischemia will result from better understanding of the basic biology of the ischemic process. Studies of the biochemical responses to ischemia and their modification may be particularly rewarding. Studies of the basic pathophysiology of myocardial ischemia will have far-reaching application in the treatment of other diseases characterized by vascular insufficiency, such as stroke and peripheral vascular disease.

2.5 HEART ATTACK: SUDDEN DEATH

At least half the deaths due to heart attack occur suddenly outside the hospital and within the first hour after the onset of symptoms. Sudden death most commonly results from a change in cardiac rhythm—by the sudden onset of a rapid abnormal rhythm or the cessation of all cardiac activity. If this change in rhythm (arrhythmia) occurs in a hospital or in the presence of trained personnel, most patients can be saved by appropriate resuscitation procedures. In the majority of instances, the suddenness of the event and the circumstances of occurrence in the home or at work minimize the possibility of such effective treatment. Therefore, the most reasonable approach to the problem is *prevention of the arrhythmia*. This must be based upon better understanding of the electrophysiology of depolarization and excitation of heart muscle and the alteration of these processes by ischemia. The relationships between the chemical structure of antiarrhythmic compounds and their function must be carefully examined. More effective preventive agents

should evolve from these studies and must be subjected to clinical trials in high-risk populations.

The availability of an animal model for human coronary heart disease would facilitate developments in this field. To be most useful, the animals would have to exhibit arrhythmia, sudden death, and myocardial infarction as consequences of vascular lesions.

Improved methods for collecting and analyzing electrocardiographic data will make it possible to acquire much needed information about the arrhythmias occurring during the first few hours of myocardial infarction. The effectiveness of emergency care systems in the management of these arrhythmias must also be evaluated.

2.6 HEART FAILURE

At least one and a half million Americans suffer from chronic heart failure and approximately one quarter of a million new cases occur each year. The problem is large in terms of disability with between 300,000 and 600,000 patients admitted to hospitals each year with this condition.

Heart failure is an important manifestation or consequence of a variety of diseases of the heart including coronary artery disease, hypertension, rheumatic and congenital heart disease. The response of the myocardium to all these disease processes involves dilatation, hypertrophy, and alteration in mechanical properties and metabolism.

Although heart failure has long been recognized as the end stage of heart disease, the mechanism of this process remains poorly understood, and treatment is still either empirical or directed at secondary manifestations, such as edema. The most effective therapeutic agents, the digitalis glycosides, have been in use since at least the 18th century. We are now just beginning to understand the way in which these drugs benefit the failing heart and how better to utilize them clinically. An important recent advance has been the ability to measure blood levels of the digitalis glycosides by new techniques of radioimmunoassay so that their clinical pharmacology may be better understood and their use in patients improved.

A major effort must be directed at understanding the contractile process of the heart, its control by the autonomic nervous system, the role of regulatory hormones and their receptors, and the determinants of myocardial oxygen consumption. Information uncovered in this research effort may be translated into fresh insights in the treatment of heart failure, such as development of new drugs and more appropriate utilization of existing forms of therapy.

2.7 RHEUMATIC AND OTHER VALVULAR DISEASES AND CARDIOMYOPATHY

Rheumatic fever is of particular importance because it is possible to prevent this disease by prompt and effective treatment of streptococcal infections. Further research on the basic biology of the streptococcus will lead to improved methods of diagnosis and treatment of beta streptococcal infection and might also eventuate in the development of an antistreptococcal vaccine. Improved therapy of streptococcal infection would also result in a reduction in the incidence of glomerulonephritis. Treatment of most types of valvular disease is available in the form of valve replacement, but there is need for better prosthetic devices constructed of improved nonthrombogenic surfaces.

Diseases of the myocardium should also be considered with emphasis on the role of nutritional factors and alcohol in the production of cardiomyopathy.

2.8 PRIORITY RECOMMENDATIONS

2.8.1 Atherosclerosis

- **Conduct clinical trials on high risk populations to determine the effectiveness of the modification of risk factors such as hyperlipidemia, hypertension, smoking and sedentary living on the prevention of atherosclerosis and its complications.**

- **Investigate the pathogenesis of atherosclerosis by studies of the basic cellular biology of the blood vessel wall and its interaction with circulating blood and its components.**

2.8.2 Thrombosis

- Conduct clinical trials of agents that inhibit platelet aggregation such as aspirin and low dose heparin in patients with coronary heart disease and cerebral vascular disease.

- Investigate the mechanism whereby intravascular thrombosis is initiated and propagated within atherosclerotic and normal blood vessels by studies of the clotting process, the wall of the blood vessels and the dynamic properties of flowing blood.

2.8.3 Hypertension

- Conduct clinical trials to determine the long term drug treatment of mild-to-moderate hypertension on the incidence of stroke and heart attack.

- Determine the causes of hypertension by research programs which would include study of the renin-angiotensin-aldosterone system, the central and peripheral autonomic nervous system, and of vascular smooth muscle.

2.8.4 Sudden Death

- Explore the electrophysiology of the ischemic heart to develop more effective antiarrhythmic drugs.

- Conduct clinical trials to determine the usefulness of prophylactic medication on reducing the incidence of sudden death in high risk populations.

- Determine the effectiveness of improved systems for the delivery of emergency medical service in reducing the incidence of sudden death.

2.8.5 Myocardial Ischemia and Infarction

- Study the means whereby the mass of ischemic and infarcted tissue resulting from vascular occlusion can be minimized by evaluating hemodynamic, mechanical, biochemical and surgical approaches.

2.8.6 Heart Failure

- Study the process of cardiac contraction and its control to develop methods to improve the function of heart muscle.

2.8.7 Vascular Lesions

- Encourage biomedical engineering efforts to develop noninvasive methods utilizing radioactive materials, ultrasound and other approaches to detect asymptomatic vascular lesions.

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III. LUNG DISEASES

3.1 EMPHYSEMA AND CHRONIC BRONCHITIS

Emphysema and chronic bronchitis are common—and still increasing—causes of death and disability in this country. As a consequence of their morbidity, approximately 100,000 man-years are lost annually to the labor force. In 1971 these diseases accounted for about 30,000 deaths. Because of their high mortality and extreme morbidity, emphysema and chronic bronchitis warrant particular attention, especially with regard to the relationship of smoking to these diseases and the evidence for a predisposition to them.

As smoking has a key role in the development of both chronic bronchitis and emphysema, it is especially important to investigate measures to modify the smoking habits of the population, and to pursue studies designed to reduce the injurious effects of tobacco on the lung. Essential to the latter type of investigation are studies to learn the mechanisms by which the lung is cleared of particles that are inhaled in smoking, how these clearance mechanisms are modified by pollutants from the environment, and, through prospective epidemiologic studies, what determines individual differences in response to the injurious effects of tobacco.

Recent investigations have shown that individuals who inherit a deficiency of a specific enzyme, alpha$_1$-antitrypsin, are predisposed to develop emphysema. This association suggests that other situations associated with accelerated enzymatic digestion of lung connective tissue may be implicated in emphysema. In addition to a systematic search for inherited enzyme abnormalities that predispose to development of obstructive lung disorders, investigations should be directed to the therapeutic possibility of neutralizing the effects of protein-digesting enzymes. Animal models of both emphysema and chronic bronchitis which are now available should be used more widely to study these disorders.

Because emphysema and chronic bronchitis are usually irreversible by the time they are diagnosed, improved techniques and devices are needed to detect early biochemical, immunologic or physiologic abnormalities associated with the development of these diseases. It is also important to determine whether airway disease in infants and children predisposes to chronic obstructive lung disease in the adult.

3.2 PULMONARY FIBROSIS

When injured as a consequence of environmental agents, infections or various other diseases, the lung may respond by depositing fibrous connective tissue—a

scar. Such pulmonary fibrosis is common to a number of diseases which constitute a group that is exceeded only by emphysema and chronic bronchitis in contributing to the morbidity and mortality from respiratory diseases.

If patients can be shielded or removed at an early stage from further exposure to the conditions that have stimulated development of pulmonary fibrosis, irreversible damage may be prevented. Hence, it is of prime importance to know more about various factors that may cause the formation of fibrous connective tissue, and also to be able to detect subtle changes in the damaged lung that may be followed by fibrosis. Sensitive pulmonary function tests, improved X-ray diagnosis, and development of biochemical and immunologic tests are approaches to early diagnosis that should be emphasized.

A better understanding of how collagen—the fibrous protein of connective tissue—is synthesized and degraded could lead to specific therapy to prevent or modify the processes that result in pulmonary fibrosis. This approach has shown promise in animal experiments where pulmonary fibrosis following exposure to silica has been prevented by specific agents.

3.3 IMMUNOLOGIC LUNG DISEASES

Lung diseases that are a consequence of immunologic abnormalities include bronchial asthma, Farmer's lung, diffuse hypersensitivity pneumonitis and sarcoidosis. Best characterized and the most prevalent of these diseases, asthma affects about nine million persons in this country, occurs in almost all age groups, and is responsible for about 5 percent of all chronic disability. Overall, the immunologic lung diseases constitute a major national health problem.

An important lead to future investigation is recent work showing that the manifestations of asthma are triggered by release of various chemical mediators from lung cells. Studies to identify other mediators, to determine where and how they act, and to learn what governs their release would provide information that is essential for the development of more effective therapy. It is also necessary to know how individuals differ in their immunologic patterns and in their responses to pharmacologic agents. As agents eliciting immunologic lung responses are airborne, it is essential both to an understanding of these diseases and to their treatment that studies be directed to the mechanisms by which the lung rids itself of inhaled micro-particles and aerosols. Also important are investigations of the properties of mucus, which may be abnormal in immunologic lung diseases.

Epidemiologic investigations are needed to learn more about the etiology and incidence of allergic bronchial diseases and the relationship of respiratory infections to their occurrence. In these diseases as in others discussed above, early detection is essential. Hence, further development of simple, accurate techniques for early diagnosis is important. Also needed are studies of: (1) the response to repeated exposures of an offending substance that precipitates an asthmatic attack, and (2) the chemical changes that characterize a particular abnormal immunological state. With the identification of chemical mediators and an understanding of physiological abnormalities, the path would be opened to the development of pharmacologic agents that should then be evaluated for their therapeutic effectiveness.

3.4 RESPIRATORY FAILURE

Respiratory failure is characterized by abnormalities of lung function and structure of such dimensions as to be lifethreatening. This may be a consequence of the natural progression of a chronic lung disease, but it may also occur in patients with previously normal lungs who suffer shock, trauma, drug overdose or a variety of other diseases. Far from rare, respiratory failure is estimated to affect about 150,000 persons a year and to have a mortality rate of 40 percent.

Critical to the prevention and treatment of acute respiratory failure is an understanding of the mechanisms that cause lung injury. Bioengineering technology has much to contribute to development and improvement of noninvasive methods for early diagnosis through continual sequential monitoring of blood oxygen, carbon dioxide, and acidity, as well as of the mechanical properties of the lung. New forms of treatment, which now include intensive diuresis, artificial ventilation and use of membrane oxygenators, should be evaluated through controlled clinical trials. Long-term follow-up studies are also needed to assess

patients recovering from respiratory distress syndromes. The development of model emergency services at the community level would be useful. But the ultimate goals of prevention and effective treatment depend upon a better understanding of the mechanisms by which the damaged lung undergoes repair.

3.5 PRIORITY RECOMMENDATIONS

- The major missing element in those diseases which comprise the bulk of pulmonary disease is knowledge of the cellular biology of lung tissue. Understanding of this would lead to major advances in chronic bronchitis, emphysema, pulmonary fibrosis, immunologic lung diseases, respiratory diseases of children and respiratory failure. Hence, studies in this area are the number one priority. More rapid progress in this area would be made by the establishment of investigative units organized to explore these basic considerations.

- It should be recognized, however, that progress will be slow in this field and that a number of palliative but specific approaches can be implemented at this time. In the case of chronic bronchitis and emphysema, programs designed to decrease smoking, particularly in the young, would make a major impact. In the case of pulmonary fibrosis, the identification of causes would lead to specific measures of prevention. In the case of allergic airways disease, studies of how individuals differ in immunologic pattern and pharmacologic response are recommended. In the case of respiratory failure, the evaluation of existing therapy and dissemination of information concerning diagnosis and treatment are recommended.

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IV. DISEASES OF CHILDHOOD

4.1 LUNG DISEASES OF INFANCY AND EARLY CHILDHOOD

Among disorders of childhood that involve the lung, hyaline membrane diseases and cystic fibrosis present health problems of national dimensions.

A disorder of the newborn usually associated with prematurity, *hyaline membrane disease* affects about 50,000 infants a year. Half of these are likely to die unless they receive specialized therapy. If successfully treated, the normal processes of lung growth and development will enable them to survive. At neonatal intensive care centers where meticulous care and sophisticated techniques are available, survival rates have been impressive. Similar centers should be developed on a regional basis, and provision should be made for rapid transfer of affected infants to these facilities.

Prevention of hyaline membrane disease can only be achieved through a better understanding of factors that contribute to premature births and of developmental processes in the normal lung. As hyaline membrane disease is characterized by general collapse of the air sacs (alveoli) of the lung, it is particularly important to study factors that can prevent this collapse. To this end, it is necessary to learn more about the role of surfactant, a substance that prevents collapse of the alveoli in the normal lung and that seems to be deficient in the infant with hyaline membrane disease. To study the premature lung, investigations should be continued in available animal models—lamb and rabbit—and extended to the prematurely delivered primate. Prenatal diagnosis, now possible through biochemical techniques, is a new approach of great promise that should be extensively exploited in further studies. To insure optimal care, criteria for treatment should be established, and pharmacologic agents that provide circulatory support or that accelerate lung maturation should be evaluated.

Cystic fibrosis, a genetically determined disease and one of the main causes of chronic illness in children and young adults, occurs in 1 in 2,000 live births and accounts for most deaths from chronic pulmonary disease in pediatric patients. The primary need is to identify the basic biochemical defects caused by the gene. This depends upon development of accurate methods of detecting and identifying abnormal factors in the body fluids and tissues of patients with the disease. Effective treatment requires an understanding of how to modify the high rate at which mucus is produced and how to modify its composition—in particular, how to reduce its viscosity. Studies of the mechanisms by which the lung rids itself of particles and fluid are especially relevant to cystic fibrosis as this disease is characterized by excessive accumulation of bronchial mucus and inability to clear the airways.

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4.2 CONGENITAL HEART DISEASES

It is estimated that 8 out of every 1,000 newborn infants have congenital heart disease. Half of the children born with congenital heart disease do not reach their first birthday, and 90 percent of the half who die in the first year do so within the first six months of life (and most of these by the third month). Thus, the neonatal period is the time of greatest risk. It is apparent, therefore, that the major focus on congenital heart disease should be the provision of early diagnosis and prompt treatment in the neonatal period. This can best be accomplished by:

- Widespread training of personnel in newborn nurseries to detect the child with congenital heart disease early in life
- Development of noninvasive diagnostic procedures to confirm the diagnosis
- Development of a regional network of facilities whereby the infant can be transferred to a cardiac diagnostic and surgical facility for prompt correction.

Surgical therapy is available for most forms of congenital heart disease, if the patient can be brought to the appropriate facility. Studies of the basic pathogenesis of congenital heart disease will provide important leads in decreasing the incidence of this group of disorders.

The similarity of management of hyaline membrane disease and congenital heart disease (early recognition, regional centers of expertise, requirements for transport of sick infants) suggests collaborative centers in which both types of problems can be managed.

4.3 HEMOPHILIA AND OTHER HEMORRHAGIC DISEASES

There are at least 25,000 patients with moderate or severe hemophilia in the U.S. The disease constitutes a major health problem for two special reasons: (1) the treatment bankrupts the patient and his family socioeconomically and emotionally, and (2) therapy, currently based upon the use of a plasma fraction obtained from human blood, represents one of the greatest single demands on the nation's blood resources.

Aside from other bleeding diseases caused by inherited defects in plasma clotting proteins and in blood platelets, hemorrhage may also develop as a result of the ingestion of many drugs, including common ones such as aspirin, in part, at least, because of the drug's effect on platelets. Finally, hemorrhage may not only occur in advanced hypertension and in association with kidney and liver failure, but it may also be aggravated in major injuries and operative procedures by an inherited or acquired hemorrhagic tendency.

Family counselling of patients with inherited bleeding disorders, home care demonstration units for hemophiliacs and improved tests to identify the causes and mechanisms whereby hemorrhage occurs are needed now. Also to be developed are improved methods for harvesting, concentrating and storing separately and without damage the platelets and specific clotting proteins, as well as red cells, so that the proper blood concentrate may be given to patients in anticipation of bleeding. To meet these various needs, further elucidation of platelet ultrastructure and the interaction of platelets with endothelium and with the plasma coagulation and fibrinolytic enzyme systems is essential.

4.4 SICKLE CELL DISEASE AND THE HEMOGLOBINOPATHIES

The hemoglobinopathies are inherited illnesses which affect the red blood corpuscles of large numbers of Americans. One out of every 400 blacks is born with sickle cell anemia, the most common and serious of these diseases. The total number of patients with sickle cell anemia is somewhat less than the estimated 50,000 to 55,000 which would be expected from the incidence at birth because of deaths of young people with the disease.

Most needed at the present time are: public education about the nature of sickle cell anemia, population screening and disease detection programs, patient and family counselling and further elucidation of the natural history of the disease. Also to be determined are the best methods of managing the secondary complications of disorders such as the sickle cell crisis. Definitive therapeutic trials of agents which

appear to have promise should be undertaken. To uncover some of these agents for clinical trial, further understanding of the molecular structure and function of hemoglobin is required.

4.5 PRIORITY RECOMMENDATIONS

4.5.1 Lung Diseases

- Hyaline membrane disease and cystic fibrosis require the development of methods of early and prenatal diagnosis and the development of regional emergency care centers where meticulous and sophisticated techniques are available, including provision for rapid transfer of affected children to these facilities.

4.5.2 Congenital Heart Diseases

- Assure the recognition of congenital heart diseases during the first few hours of life by the training of nurses and other persons who work in newborn nurseries. Early recognition must be followed by prompt transfer to specialized facilities for diagnosis and treatment.

4.5.3 Hemophilia

- Improved methods are needed in regard to the harvesting, concentrating and storing of factor VIII or effective biological or synthetic substitutes.
- The effectiveness of prophylactic therapeutic programs and of home care units should be carefully evaluated.
- Genetic counselling should provide advice on marriage, children, occupation and emotional adjustments to patients with hemophilia.

4.5.4 Hemoglobinopathies

- Fundamental research is urgently needed to uncover agents suitable for clinical trials in the prevention of the sickling phenomenon and the treatment of sickle cell crisis.
- Improved methods should be developed for the management of the secondary complications of sickle cell anemia including sickle cell crisis.
- Public education is required concerning sickle cell anemia and sickle cell trait.
- The application of current tests and the development of new techniques to facilitate population screening for sickle cell disease and trait should be encouraged.
- Genetic counselling should provide advice on marriage, children, occupation and emotional adjustments to patients with hemoglobinopathies.

V. BLOOD RESOURCES AND TRANSPLANTATION

5.1 BLOOD RESOURCES

5.1.1 A Nationwide Blood Bank System

An ample supply of high quality blood and blood products is essential to the nation's health. The existing system for providing these services is fragmented, unplanned, and poorly managed. It results in maldistribution, waste, and excessive cost, and compromises quality and safety. The Panel Chairmen strongly recommend that, in a stepwise fashion, a network of regional blood centers coordinated at the national level be developed. The regional blood centers should function as comprehensive community health facilities responsible for all blood, blood components and blood services needed by patients in the geographical area served. The regional centers should, in addition, have the capacity (depending upon size and location) to conduct research and training programs, to provide resources for tissue typing and organ recruitment and preservation for transplantation, and to make available special facilities for the management of clinical problems in blood coagulation and for other clinical and diagnostic purposes. In order to function effectively and provide a much needed scientific base for the nation's blood resource, the regional blood centers should be located in proximity to, and have a close organic relation with, universities, hospitals, or medical centers.

The regional blood centers do not by themselves constitute a coordinated blood bank system. They need to be woven into an effective nationwide network for purposes of overall planning, better utilization of blood resource, and more efficient management. This vital integrating function can and should be performed by a consortium of the three existing national blood bank organizations (American Association of Blood Banks, American National Red Cross, and Council of Community Blood Centers).

A prime responsibility of the unified system is the development of a vigorous year-round nationwide campaign for the recruitment of voluntary blood donors. At the outset this will necessarily use existing knowledge and resources for public education and information. However, social and psychological studies of donor motivation and organization will be necessary to expand the program, to broaden public participation, and to make it more cost-effective.

Training programs are urgently needed to meet the acute and growing shortage of qualified physicians to staff the nation's hospital blood banks and regional blood centers. Without such trained and highly specialized personnel, regionalization will be delayed and the quality of transfusion services to patients will suffer.

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An essential element of the nationwide system is the creation of a National Blood Data Center, whose functions would be to:

- Gather, in an organized way, the statistical information on collection, usage, out-dating, component production, etc., without which it would be impossible to monitor the system or to plan effectively
- Engage in operations research to improve the system and to assess the impact on the blood resource of population trends, social changes, and the introduction of new therapeutic procedures
- Maintain ongoing surveillance of the system from the point of view of supply, cost, and the possible transmission of disease.

5.1.2 Hepatitis

Hepatitis is the most frequent serious complication encountered in transfusing blood and blood products. Post-transfusion hepatitis is estimated to occur annually in 20,000 to 30,000 patients and to be fatal in about 3,000. The recent discovery of an antigen closely related to the hepatitis virus and the development of tests which, though still imperfect, can detect carriers of the disease have for the first time provided tools with which it may now be possible to prevent post-transfusion hepatitis. However, it has become apparent that hepatitis is a much larger public health problem than previously suspected. The new tests have brought to light the fact that there are approximately 500,000 to 1,000,000 chronic carriers of the hepatitis virus in the country, only a very small proportion of whom can be accounted for by blood transfusion or drug addiction. How they contract the disease and the nature of the risk to themselves and to others is still largely unknown. There is urgent need for a concerted attack on hepatitis not just as a complication of blood transfusion, but as a major public health and social problem. This attack should include more sensitive practical tests for detecting the carrier state, studies on the epidemiology and treatment of the carrier state and the relation of the carrier state to cirrhosis of the liver and liver cancer, and the development of animal systems or *in vitro* tests for recognition of infectious virus. High-titer, specific immunoglobulins against hepatitis B virus now exist in limited quantities, and there is preliminary evidence that heat-treated virus retains its antigenicity. Both these observations warrant a full-scale program to develop passive immunization and active vaccination against this disease.

5.1.3 Blood Components and Plasma Derivatives

Blood components (such as red cells, platelets, and granulocytes) and plasma derivatives (such as albumin, immunoglobulins, and factor VIII) are being used increasingly in more rational and more effective treatment of disease. However, the methods for producing these important therapeutic agents are still primitive, and in some cases—notably that of factor VIII, which is essential for the treatment of hemophilia—they are both costly and wasteful. There is need for: (1) studies on the metabolism of the formed elements of the blood to learn the best conditions for their separation and long-term preservation, and (2) careful clinical studies to develop clear indications for their use and for better methods to assess their effectiveness in patients.

The plasma fractionation methods being used today are those developed prior to World War II. They have made available only a limited number of clinically useful products, and these at relatively low yield and high cost. The field needs to be revitalized by establishing specialized research and development centers with capabilities in protein chemistry and plasma separation whose mission would be: (1) to devise new methods for plasma protein fractionation, (2) to develop more efficient methods for purifying factor VIII, (3) to isolate new plasma proteins that may have clinical or laboratory usefulness, and (4) to train requisite scientific and engineering manpower.

5.1.4 Priority Recommendations

- **Create a national blood bank system based upon a coordinated network of regional blood centers. This should be given high priority because its achievement will result in more effective use of the nation's blood resources and will maximize the opportunity for successful accomplishment of the ensuing recommendations.**

- Mount a concerted attack on hepatitis as a serious public health problem. The attack should include the development and use of more sensitive practical tests for detecting the carrier state, studies of the biology and epidemiology of the carrier state, and a coordinated program to develop passive immunization and active vaccination for this disease.

- Conduct a vigorous year-round national recruitment campaign to achieve a totally voluntary blood supply. Social and psychological studies of donor motivation and organization will be necessary to broaden public participation, to extend the concept of voluntarism to plasmapheresis and cytopheresis, and to make the system cost effective.

- Expand the scientific base by creating scientific centers of excellence for research and development in regional blood centers closely associated with universities or major medical installations. Plasma fractionation is an area that deserves particular emphasis in this connection.

- Relieve the acute and growing shortage of qualified physicians needed to staff the nation's hospital blood banks and regional blood centers. Training programs are urgently needed to develop the highly specialized medical manpower without which regionalization will be delayed and the quality of transfusion services to patients will suffer.

- Create a National Blood Data Center.

5.2 TRANSPLANTATION

5.2.1 Support for Transplantation Research

Wider and more effective use of transplanted human tissues and organs will require better understanding of the underlying genetic and immunologic factors that cause graft rejection. Support for transplantation biology and the scientific disciplines related to it is, therefore, of high priority. In addition, there is need for the creation of transplant research centers to stimulate interdisciplinary approaches to both clinical and basic transplantation problems and to train personnel.

5.2.2 Regional and National Programs for Organ Procurement

Kidney transplantation is an accepted therapeutic procedure. As new knowledge emerges from the research laboratories, the transplantation of other organs and tissues will become practical also. There is need to develop an effective network of centers on a regional and national basis that would:

- Extend the public's knowledge of the ethical, legal and medical issues in transplantation of human organs

- Initiate an appropriate educational and recruitment effort to procure the needed organs and tissues

- Develop acceptable criteria for the distribution of organs

- Serve as central repositories for donor and recipient clinical and laboratory data, and for the performance of essential typing and cross-matching procedures. Many regional blood centers will have the requisite resources and personnel to serve also as regional transplant centers.

5.2.3 Improved Clinical Management of the Transplant Patient

Successful transplantation of human organs has brought with it a series of new problems that need to be investigated, such as: (1) development of better and more specific immunosuppressive agents, (2) prevention of graft-versus-host reactions, (3) prevention and treatment of infection, (4) recurrence of the original disease, and (5) increased susceptibility to cancer.

5.2.4 Organ Preservation

Kidney transplantation is seriously hampered at the present time because of the very limited storage life of

organs—a matter of hours to a very few days. Extending the storage life of organs to weeks, months, or perhaps indefinitely, would enormously increase the available supply, make it possible to transport organs readily across the country (or even internationally), improve greatly the chances for an optimal match between donor and recipient, and convert what is now often a hectic emergency operative procedure into a routine elective one. Promising leads involving low temperature storage, perfusion under various conditions, and organ culture should be explored.

5.2.5 Priority Recommendations

- Expand the support for fundamental research in immunology, immunogenetics and other aspects of transplantation biology
- Improve clinical management of the post-transplant state, such as prevention of graft-versus-host reaction, the development of better immunosuppressive techniques, and the prevention and treatment of infection
- Promote public dialogue on the ethical and legal problems associated with organ transplantation
- Develop regional and national programs for organ procurement, wherever possible in conjunction with the proposed regional blood centers
- Develop improved procedures for organ preservation and storage.

VI. GENERAL CONSIDERATIONS

During the discussions and deliberations that were required for the preparation of this report, it became apparent that certain conclusions and precepts had wide applicability. Indeed, these concepts and judgments appeared to be so comprehensive and fundamental that they warrant emphasis in this special and concluding section. These salient principles involve:

- Needs for skilled manpower
- Education of the public
- Evaluation of new therapies
- Development of better ambulatory care methods
- Demonstration projects
- Specialized facilities.

6.1 NEEDS FOR SKILLED MANPOWER

An essential element in a planned effort designed to control heart, lung, and blood diseases is the provision of trained manpower. Training to perform the basic services and to conduct the needed research is indispensable for long-range progress. Trained individuals, of many types and disciplines, are needed to carry out the program suggested, to complete and accomplish the needed work already underway, and to attain the ultimate objectives. The effective use of facilities, equipment, and other resources requires motivated, dedicated, and highly trained personnel. To date, our country has been most fortunate in this regard. The need for trained individuals has been recognized and acknowledged, and funds for these purposes have been available.

Therefore, effective implementation of this program will require continuing and more precise estimates of the need for trained people. This process of critical assessment and evaluation is difficult, but it is a vital prerequisite for effective planning. In part, the difficulty derives from the fact that training is a slow, long-term, and sometimes inefficient process. The conversion of a medical school graduate into a trained investigator requires at least five years of specialized study beyond medical school. Advanced planning is, therefore, essential. Long-term needs for personnel at all levels should be determined, and the individuals should be trained to meet those needs.

Discoveries that are essential for the conquest of atherosclerosis and hypertension, similar to those which have eliminated poliomyelitis, can be made only by trained scientists. New therapeutic procedures and devices can be tested and evaluated only by clinical

investigators skilled in the application of scientific disciplines to the assessment of results in patients. Implementation of an expanded program on heart, blood vessel, lung and blood diseases, and blood resources and the delivery of improved medical services to the community requires physicians, nurses, and other allied health professionals.

An attempt should be made to quantitate current and future needs for trained manpower. There is need for both investigators and practitioners, and training programs must be designed appropriately to meet both requirements. For example, the Panels have clearly identified a need for additional specialists in the field of peripheral vascular disease and in blood banking. This and needs in other specialized areas should be evaluated, and appropriate programs should be developed.

It is recognized that there are training needs for many types of personnel. For example, the implementation of programs for the detection and treatment of hypertension in the community can be implemented only if a large number of allied health professionals is available. The problem of community information and motivation also requires health volunteers who will provide a network to deliver the health message to the people.

Continuing education at all levels should be encouraged. As new information becomes available, it must be delivered to practicing physicians and allied health professionals. An effective process of information-renewal and updating is mandatory. The training process never ceases. Thus, continuing education must be built into the health delivery system.

Training, like the acquisition of new knowledge through research, is an investment in the future which cannot be ignored.

6.2 EDUCATION OF THE PUBLIC

The success of new programs to control heart, lung, and blood diseases and to provide blood resources will depend in large measure upon greater awareness, understanding, and acceptance on the part of the public. If the health profession expects the public to change its eating or smoking habits or to participate more enthusiastically in voluntary blood donations, improved methods must be developed for communicating with the public and for gaining its confidence. It will be necessary to make better use of the voluntary health agencies and the existing communications media, and to begin the educational process early in life. In addition, it will be desirable to develop new and more effective techniques for improving public awareness. This will require broad research programs by skilled social scientists, psychologists, and experts in motivation and communication. The public must be more than a passive recipient of health care. It should be an informed and willing participant, and the tools to do this must be developed in a systematic and socially acceptable way.

6.3 EVALUATION OF NEW THERAPIES

A continuing committee within the NHLI is needed to formulate and implement strategy for the evaluation of new therapy coming within its purview. In regard to drug treatment and the use of devices in therapy, this committee should facilitate close collaboration between the NHLI staff, other interested governmental agencies including the FDA and outside scientists (academic and industrial) with demonstrated experience in trial design, biostatistics, clinical pharmacology, the appropriate disease areas and the relevant therapeutic modalities. The skill required here is to test the therapeutic agent after its safety and potential efficacy have gained scientific validation, but before it acquires entry into the marketplace.

Coordinated input from appropriate governmental and nongovernmental sources will minimize the hazards and maximize the gains of research—all at decreased risk to patients and cost to the country.

6.4 DEVELOPMENT OF BETTER AMBULATORY CARE METHODS

Impressive advances have been made in ambulatory care techniques. Many types of therapy that previously were available only in hospitals can now be delivered in doctors' offices, outpatient clinics, or even at home. The potential for further advances of this type is great and deserves increased attention. If a greater number of diagnostic and therapeutic activities can be conducted on an ambulatory basis (without

need for a hospital bed), there will be major economies in the prevention and treatment of disease, and there will be significant social and psychological benefits for the patient and his family.

Outpatient diagnosis, treatment, and follow-up centers can be particularly valuable and efficient for many different types of patients. Therapy for most hypertensive patients can be prescribed and adjusted in such a manner. Most patients with cardiac failure can be treated effectively on an ambulatory basis. Several centers have demonstrated the value of out-of-hospital evaluation and therapy for patients at high risk for coronary artery disease.

Earlier discharge from hospital and subsequent home care has become almost routine for patients who have had a heart attack. Prolonged (six weeks) hospitalization is now infrequent.

Increasingly, diagnostic and therapeutic procedures for bronchial asthma and other lung diseases are conducted in the physician's office and the outpatient clinic. To a considerable and rewarding extent, the discipline of rehabilitation has focused upon outpatient resources. In the area of blood diseases, home care programs have been developed for hemophilic patients—including injections of cryoprecipitates to prevent hemorrhage. This has decreased the need for prolonged and expensive hospitalization and has reduced the need for complex, rehabilitative surgery.

These ambulatory care techniques are promising and deserve further development. They can diminish the absence of the patient from his family, his community, and from his job.

6.5 DEMONSTRATION PROJECTS

All too often promising leads in health care or in the prevention of disease result in great pressures for instant and widespread implementation. It is of great importance to provide a mechanism for limited, controlled, and critically evaluated demonstration projects before new ideas are broadly instituted. Objective evaluation of these innovations should be conducted by critical, independent scientists in accordance with previously agreed upon criteria. For example, the notion that a hepatitis registry will reduce the incidence of transfusion hepatitis should be subjected to test in one region of the country before elaborate, computerized national registries are established. And, the often expressed idea that the mortality from acute heart attacks can be reduced by specially equipped and manned ambulances or by life support stations in areas of high population density should be objectively evaluated by a few demonstration projects before the number of such programs proliferate across the country. Well-conceived demonstration projects will conserve limited resources, save money, and reduce the frustration that inevitably results from premature and ill-conceived projects. They will ensure that new programs are well-tested before they are committed to general use.

6.6 SPECIALIZED FACILITIES

There is and there will continue to be a need to establish specialized facilities to conserve rare resources and to provide backup support for quality health care programs. These facilities will serve a broad spectrum of needs and there will be few in number in any one field. In some instances, there will be one-of-a-kind facilities and they will be subject to annual review concerning their effectiveness. The following possible facility needs have been abstracted from the four Panel Reports: regional blood centers, cardiac rehabilitation centers, units to evaluate circulatory assist devices, specialized facilities together with communication and transportation support for children with special cardiopulmonary problems, a reference laboratory for the diagnosis of rare blood diseases, and special animal colony resources including primate centers for research in heart, lung and blood diseases.

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